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TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	DEC 05	CASREACT(R) - Over 10 million reactions available
NEWS	4	DEC 14	2006 MeSH terms loaded in MEDLINE/LMEDLINE
NEWS	5	DEC 14	2006 MeSH terms loaded for MEDLINE file segment of TOXCENTER
NEWS	6	DEC 14	CA/CAplus to be enhanced with updated IPC codes
NEWS	7	DEC 21	IPC search and display fields enhanced in CA/CAplus with the IPC reform
NEWS	8	DEC 23	New IPC8 SEARCH, DISPLAY, and SELECT fields in USPATFULL/ USPAT2
NEWS	9	JAN 13	IPC 8 searching in IFIPAT, IFIUDB, and IFICDB
NEWS	10	JAN 13	New IPC 8 SEARCH, DISPLAY, and SELECT enhancements added to INPADOC
NEWS	11	JAN 17	Pre-1988 INPI data added to MARPAT
NEWS	12	JAN 17	IPC 8 in the WPI family of databases including WPIFV
NEWS	13	JAN 30	Saved answer limit increased
NEWS	14	JAN 31	Monthly current-awareness alert (SDI) frequency added to TULSA
NEWS	15	FEB 21	STN AnaVist, Version 1.1, lets you share your STN AnaVist visualization results
NEWS	16	FEB 22	Status of current WO (PCT) information on STN
NEWS	17	FEB 22	The IPC thesaurus added to additional patent databases on STN
NEWS	18	FEB 22	Updates in EPFULL; IPC 8 enhancements added
NEWS	19	FEB 27	New STN AnaVist pricing effective March 1, 2006
NEWS	20	FEB 28	MEDLINE/LMEDLINE reload improves functionality
NEWS	21	FEB 28	TOXCENTER reloaded with enhancements
NEWS	22	FEB 28	REGISTRY/ZREGISTRY enhanced with more experimental spectral property data
NEWS	23	MAR 01	INSPEC reloaded and enhanced
NEWS	24	MAR 03	Updates in PATDPA; addition of IPC 8 data without attributes

NEWS EXPRESS FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
http://download.cas.org/express/v8.0-Discover/

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NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 14:06:55 ON 07 MAR 2006

=>
Uploading
THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE
Do you want to switch to the Registry File?
Choice (Y/n):
Switching to the Registry File...
Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 14:07:10 ON 07 MAR 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 6 MAR 2006 HIGHEST RN 876011-49-3
DICTIONARY FILE UPDATES: 6 MAR 2006 HIGHEST RN 876011-49-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

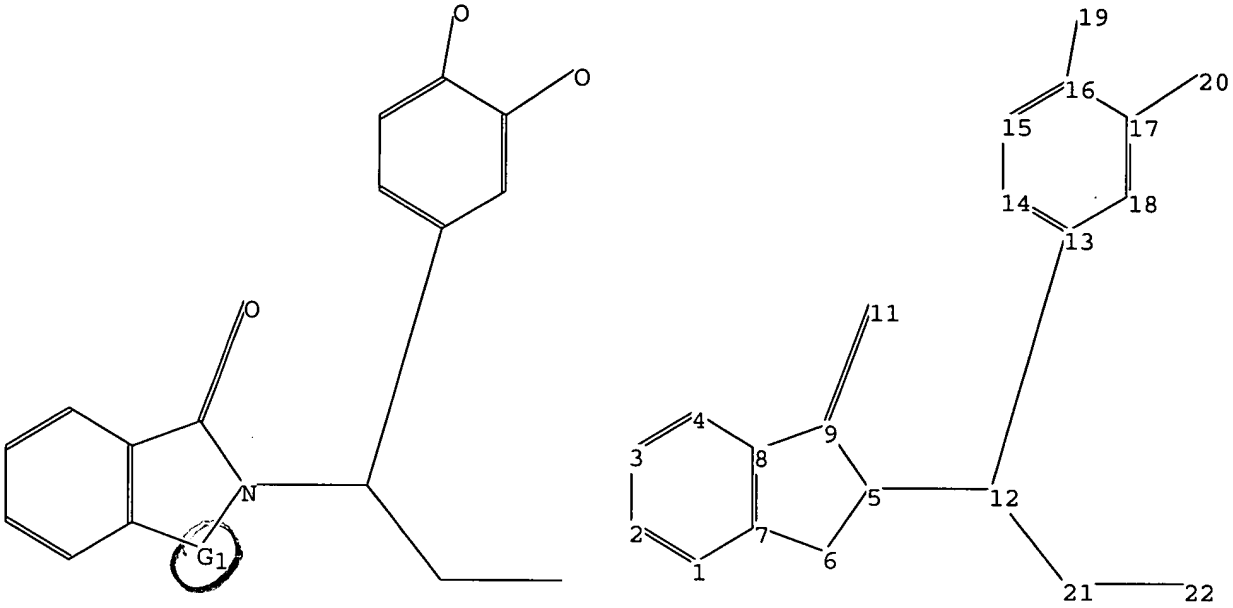
****
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\10748085.str



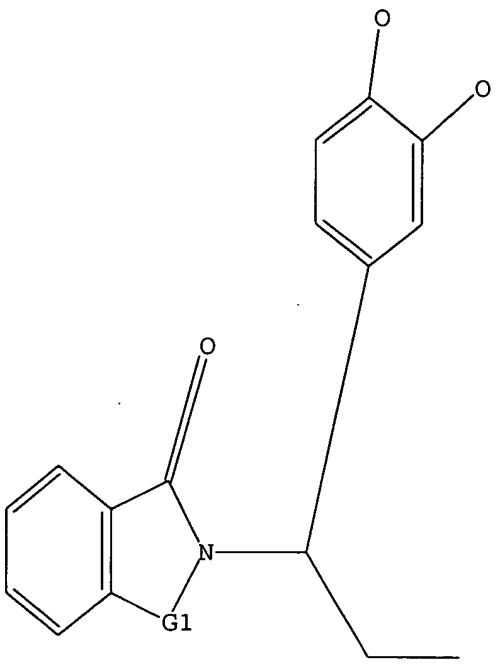
chain nodes :
11 12 19 20 21 22
ring nodes :
1 2 3 4 5 6 7 8 9 13 14 15 16 17 18
chain bonds :
5-12 9-11 12-13 12-21 16-19 17-20 21-22
ring bonds :
1-2 1-7 2-3 3-4 4-8 5-6 5-9 6-7 7-8 8-9 13-14 13-18 14-15 15-16 16-17 17-18
exact/norm bonds :
5-6 5-9 5-12 6-7 8-9 9-11 12-13 12-21 16-19 17-20 21-22
normalized bonds :
1-2 1-7 2-3 3-4 4-8 7-8 13-14 13-18 14-15 15-16 16-17 17-18
isolated ring systems :
containing 1 : 13 :

G1:CH2,SO2,C(O)CH3

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 11:CLASS 12:CLASS 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS 20:CLASS 21:CLASS 22:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 CH2,SO2,C(O)CH3

Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 14:07:27 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 22 TO ITERATE

100.0% PROCESSED 22 ITERATIONS 3 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 159 TO 721
PROJECTED ANSWERS: 3 TO 163

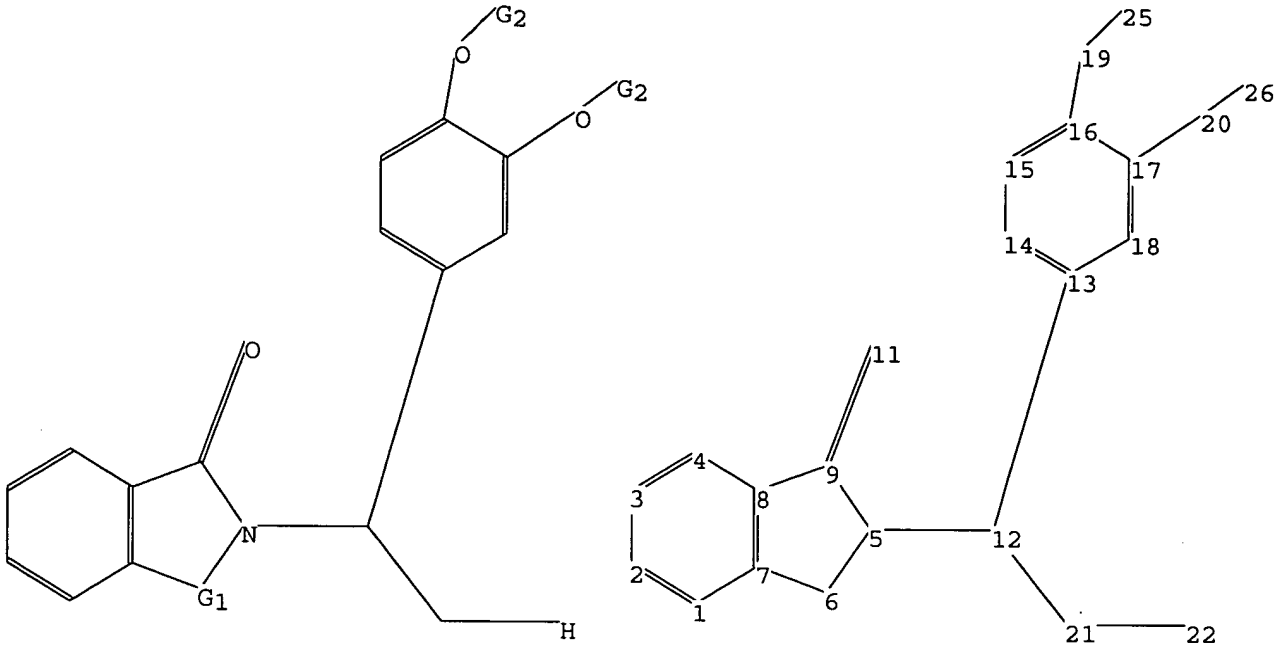
L2 3 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 14:07:35 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 586 TO ITERATE

100.0% PROCESSED 586 ITERATIONS 115 ANSWERS
SEARCH TIME: 00.00.01

L3 115 SEA SSS FUL L1

=>
Uploading C:\Program Files\Stnexp\Queries\10748085a.str



chain nodes :
11 12 19 20 21 22 25 26
ring nodes :
1 2 3 4 5 6 7 8 9 13 14 15 16 17 18
chain bonds :
5-12 9-11 12-13 12-21 16-19 17-20 19-25 20-26 21-22
ring bonds :
1-2 1-7 2-3 3-4 4-8 5-6 5-9 6-7 7-8 8-9 13-14 13-18 14-15 15-16 16-17
17-18
exact/norm bonds :
5-6 5-9 5-12 6-7 8-9 9-11 12-13 12-21 16-19 17-20 19-25 20-26 21-22
normalized bonds :
1-2 1-7 2-3 3-4 4-8 7-8 13-14 13-18 14-15 15-16 16-17 17-18
isolated ring systems :
containing 1 : 13 :

G1:CH2,SO2,C(O)CH3

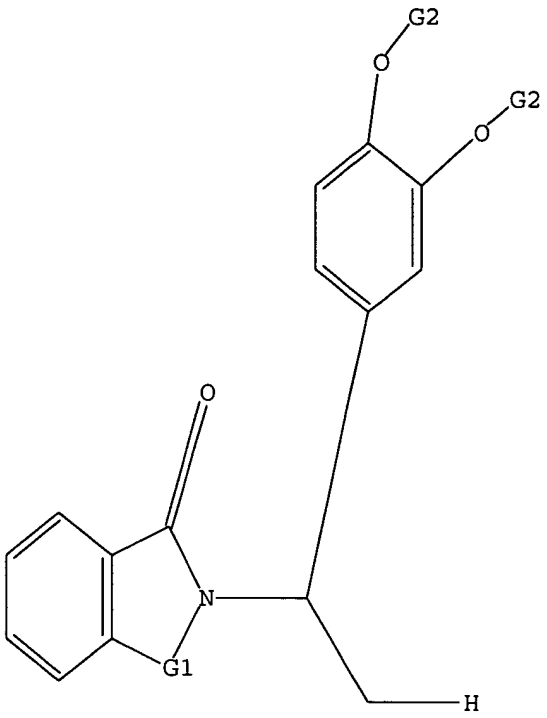
G2:CH,Cb,Ak

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 11:CLASS
12:CLASS 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS 20:CLASS
21:CLASS 22:CLASS 25:CLASS 26:CLASS

L4 STRUCTURE UPLOADED

=> d l4
L4 HAS NO ANSWERS

L4 STR



G1 CH2,SO2,C(O)CH3

G2 CH,Cb,Ak

Structure attributes must be viewed using STN Express query preparation.

```
=> s l4
SAMPLE SEARCH INITIATED 14:10:25 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -       31 TO ITERATE

100.0% PROCESSED       31 ITERATIONS                              4 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          286 TO      954
PROJECTED ANSWERS:               4 TO      200

L5            4 SEA SSS SAM L4

=> s l4 sss full
FULL SEARCH INITIATED 14:10:33 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -      772 TO ITERATE

100.0% PROCESSED      772 ITERATIONS                            149 ANSWERS
SEARCH TIME: 00.00.01

L6          149 SEA SSS FUL L4

=> FIL CAPLUS
```

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	335.64	335.85

FILE 'CAPLUS' ENTERED AT 14:10:38 ON 07 MAR 2006
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FILE COVERS 1907 - 7 Mar 2006 VOL 144 ISS 11
FILE LAST UPDATED: 6 Mar 2006 (20060306/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

```
=> d his

     (FILE 'HOME' ENTERED AT 14:06:55 ON 07 MAR 2006)

     FILE 'REGISTRY' ENTERED AT 14:07:10 ON 07 MAR 2006
L1              STRUCTURE UPLOADED
L2            3 S L1
L3          115 S L1 SSS FULL
L4              STRUCTURE UPLOADED
L5            4 S L4
L6          149 S L4 SSS FULL

     FILE 'CAPLUS' ENTERED AT 14:10:38 ON 07 MAR 2006

=> s l3
L7          39 L3

=> s l4
   REG1stRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.



SAMPLE SEARCH INITIATED 14:10:57 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -       31 TO ITERATE

100.0% PROCESSED       31 ITERATIONS                          4 ANSWERS
SEARCH TIME: 00.00.01
```

```
FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          286 TO      954
PROJECTED ANSWERS:               4 TO      200

L8            4 SEA SSS SAM L4


L9            3 L8

=> FIL HCAPLUS
COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.46     337.21

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FILE COVERS 1907 - 7 Mar 2006  VOL 144 ISS 11
FILE LAST UPDATED: 6 Mar 2006  (20060306/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> d his

     (FILE 'HOME' ENTERED AT 14:06:55 ON 07 MAR 2006)

     FILE 'REGISTRY' ENTERED AT 14:07:10 ON 07 MAR 2006
L1              STRUCTURE UPLOADED
L2            3 S L1
L3          115 S L1 SSS FULL
L4              STRUCTURE UPLOADED
L5            4 S L4
L6          149 S L4 SSS FULL

     FILE 'CAPLUS' ENTERED AT 14:10:38 ON 07 MAR 2006
L7           39 S L3
                S L4

     FILE 'REGISTRY' ENTERED AT 14:10:56 ON 07 MAR 2006
L8            4 S L4
```

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     FILE 'CAPLUS' ENTERED AT 14:10:57 ON 07 MAR 2006
L9            3 S L8

     FILE 'HCAPLUS' ENTERED AT 14:11:15 ON 07 MAR 2006

=> s l3
L10          39 L3

=> s l6
L11          41 L6

=> s l11 and pde4
          1075 PDE4
L12           8 L11 AND PDE4

=> d l12 ibib abs hitstr tot

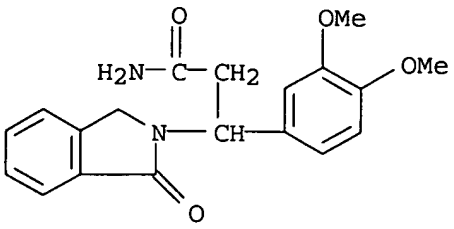
L12  ANSWER 1 OF 8  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2005:1155544  HCAPLUS
DOCUMENT NUMBER:          143:416245
TITLE:                    Methods of using, and compositions comprising,
                          phosphodiesterase 4 (PDE4) modulators for
                          the treatment and management of pulmonary hypertension
INVENTOR(S):              Zeldis, Jerome B.
PATENT ASSIGNEE(S):       USA
SOURCE:                   U.S. Pat. Appl. Publ., 33 pp.
                          CODEN: USXXCO
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     US 2005239867         A1    20051027    US 2005-111187          20050421
     WO 2005102317         A1    20051103    WO 2005-US13597         20050421
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
             NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,
             SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,
             ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
             RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
             MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:                        US 2004-565174P     P  20040423
OTHER SOURCE(S):          MARPAT 143:416245
AB   Methods of treating, preventing, and managing pulmonary hypertension are
     disclosed. Specific methods encompass the administration of a
     PDE4 modulator, or a pharmaceutically acceptable salt, solvate
     (e.g., hydrate), stereoisomer, clathrate, or prodrug thereof, alone or in
     combination with a second active agent, surgery and/or lung
     transplantation. Specific second active agents are capable of reducing
     pulmonary artery pressure. Pharmaceutical compns., single unit dosage
     forms, and kits suitable for use in methods of the invention are also
```

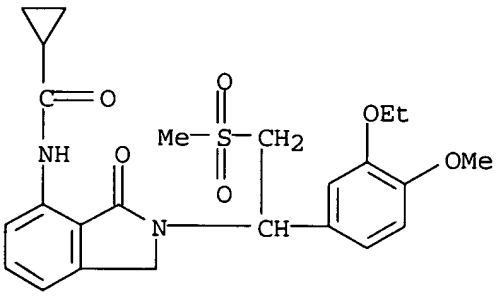
disclosed.

IT **167886-76-2 340019-67-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phosphodiesterase 4 modulators for treatment of pulmonary hypertension)

RN 167886-76-2 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



RN 340019-67-2 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)



L12 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:451120 HCAPLUS
DOCUMENT NUMBER: 142:476229
TITLE: Methods of using and compositions comprising **PDE4** modulators for the treatment and management of asbestos-related diseases and disorders
INVENTOR(S): Zeldis, Jerome B.
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005046592	A2	20050526	WO 2004-US37082	20041104
WO 2005046592	A3	20051215		

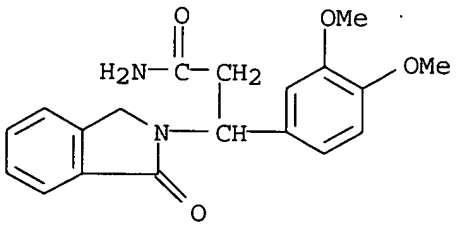
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005142104 A1 20050630 US 2004-981190 20041103
PRIORITY APPLN. INFO.: US 2003-518603P P 20031106
OTHER SOURCE(S): MARPAT 142:476229

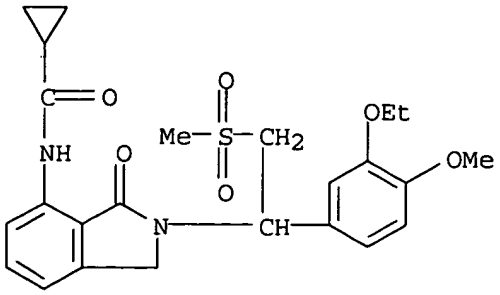
AB Methods of treating, preventing and managing an asbestos-related disease or disorder are disclosed. Specific embodiments encompass the administration of a **PDE4** modulator, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in combination with a second active agent and/or chemotherapy, surgery, or radiation therapy. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in the methods of the invention are also disclosed. Treatment with 400 mg 3-(3,4-dimethoxyphenyl)-3-(1-oxo-1,3-dihydroisoindol-2-yl)propionamide as a continuous oral daily dose is well-tolerated.

IT **167886-76-2 340019-67-2**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as **PDE4** modulator; **PDE4** modulators and compns. for treatment and management of asbestos-related diseases and disorders)

RN 167886-76-2 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



RN 340019-67-2 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)



L12 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:780510 HCAPLUS
DOCUMENT NUMBER: 141:277486
TITLE: A preparation of 7-aminoisoindolone derivatives
INVENTOR(S): Man, Hon-Wah; Muller, George W.; Zhang, Weihong
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004080423	A2	20040923	WO 2004-US7743	20040312
WO 2004080423	A3	20041104		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2518584	AA	20040923	CA 2004-2518584	20040312
US 2004254214	A1	20041216	US 2004-798317	20040312
EP 1605896	A2	20051221	EP 2004-720448	20040312
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				

PRIORITY APPLN. INFO.: US 2003-454155P P 20030312
WO 2004-US7743 W 20040312
OTHER SOURCE(S): MARPAT 141:277486
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

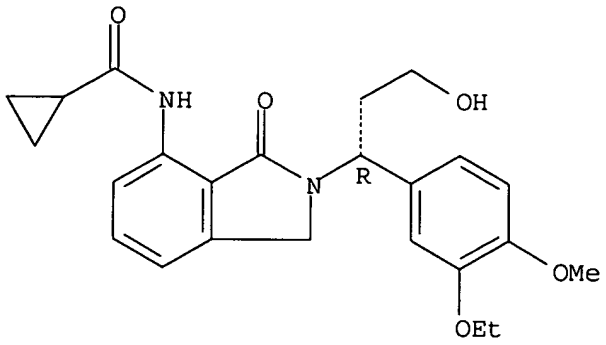
AB The invention relates to a preparation of 7-aminoisoindole derivs. of formula I [wherein: Y is C(O), CH2, CH2C(O), or SO2; X is H; Z is -alkyl-CO2H,

alkyl, -alkyl-OH, or -alkyl-NH2, etc.; R1 and R2 are independently selected from (cyclo)alkyl or -alkyl-cycloalkyl], useful for treatment, prevention or management of cancer, inflammatory bowel disease, and myelodysplastic syndrome, etc. (no biol. data). For instance, isoindole derivative II was prepared via heterocyclization of aminopropanol derivative III and benzoic acid derivative IV with a yield of 64% (example 1).

IT **760958-78-9P 760958-80-3P 760958-88-1P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of aminoisoindolone derivs. via heterocyclization of aminopropanol derivs. and benzoic acid derivs.)

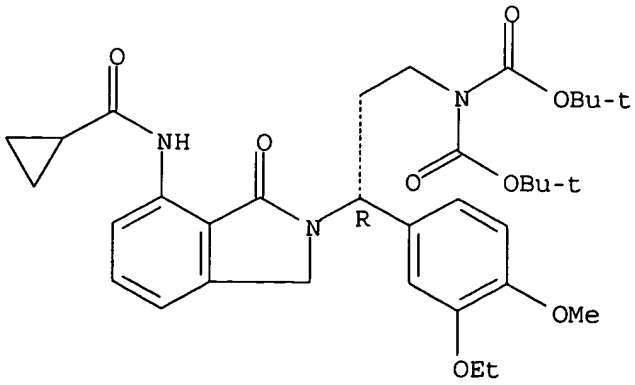
RN 760958-78-9 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-hydroxypropyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



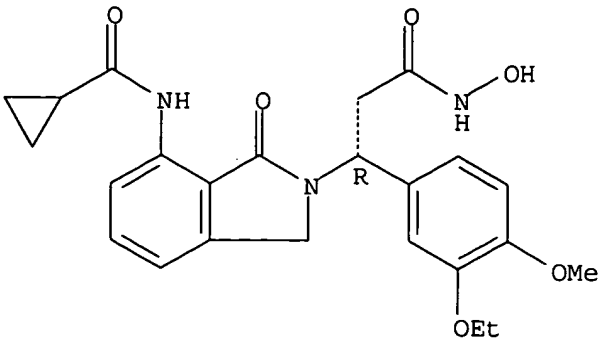
RN 760958-80-3 HCAPLUS
CN Imidodicarbonic acid, [(3R)-3-[7-[(cyclopropylcarbonyl)amino]-1,3-dihydro-1-oxo-2H-isoindol-2-yl]-3-(3-ethoxy-4-methoxyphenyl)propyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 760958-88-1 HCAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N-hydroxy-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

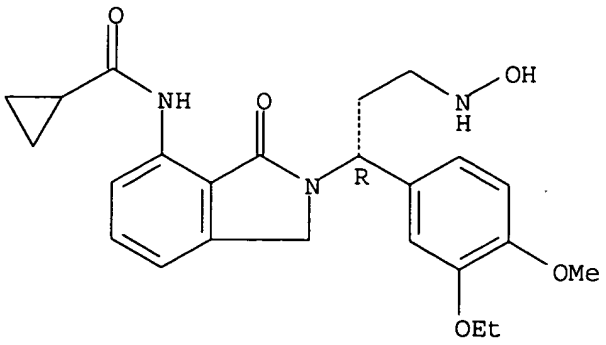


IT **760958-82-5P 760958-83-6P 760958-85-8P**
760958-86-9P 760958-87-0P 760958-90-5P
760958-91-6P 760958-93-8P 760958-96-1P
760958-97-2P 760958-98-3P 760958-99-4P
760959-00-0P 760959-03-3P 760959-04-4P
760959-06-6P 760959-07-7P 760959-09-9P
760959-12-4P 760959-13-5P 760959-14-6P
760959-15-7P 760959-16-8P 760959-18-0P
760959-20-4P 760959-22-6P 760959-23-7P
760959-24-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminoisoindolone derivs. via heterocyclization of aminopropanol derivs. and benzoic acid derivs.)

RN 760958-82-5 HCAPLUS

CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-(hydroxyamino)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

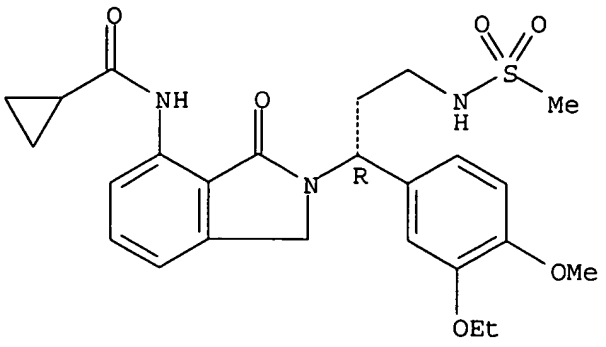
Absolute stereochemistry.



RN 760958-83-6 HCAPLUS

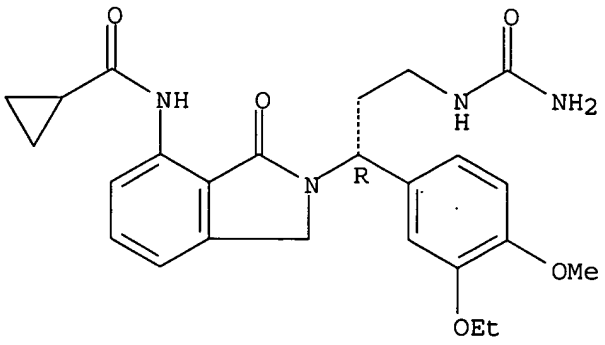
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-[(methylsulfonyl)amino]propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



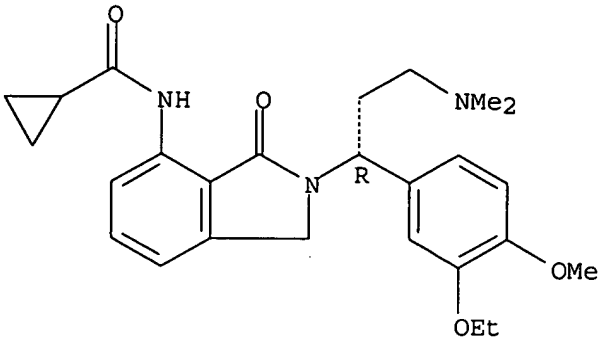
RN 760958-85-8 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-3-[(aminocarbonyl)amino]-1-(3-ethoxy-4-methoxyphenyl)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 760958-86-9 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-3-(dimethylamino)-1-(3-ethoxy-4-methoxyphenyl)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]-, monohydrochloride (9CI) (CA INDEX NAME)

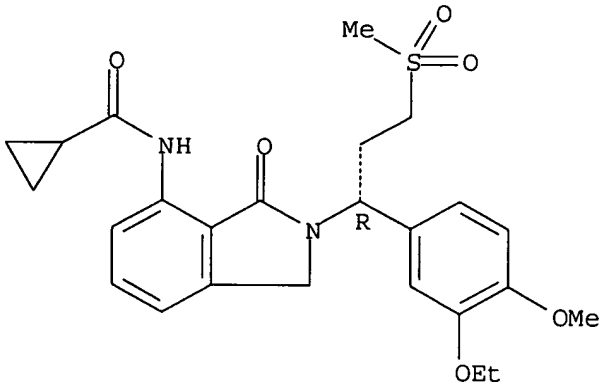
Absolute stereochemistry.



● HCl

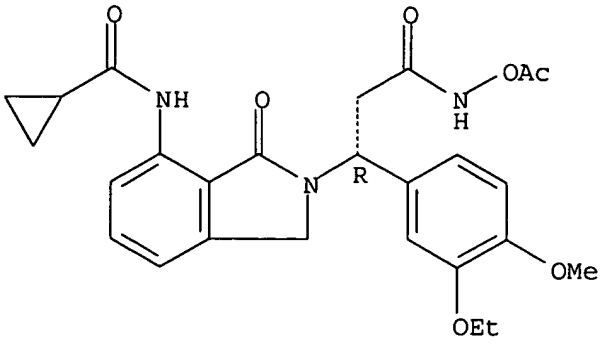
RN 760958-87-0 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-(methylsulfonyl)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



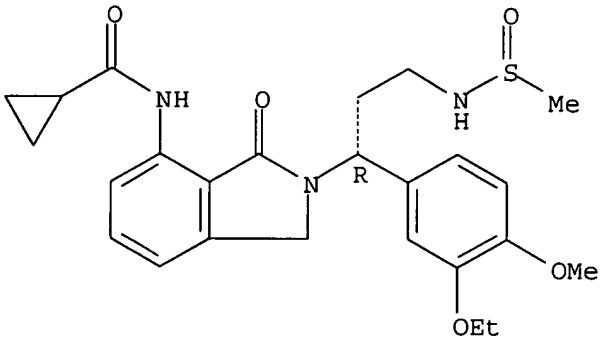
RN 760958-90-5 HCAPLUS
CN 2H-Isoindole-2-propanamide, N-(acetyloxy)-7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



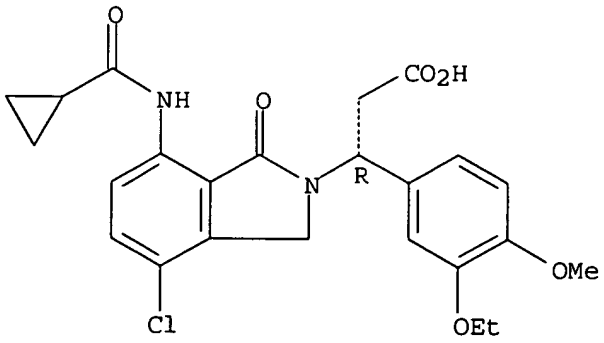
RN 760958-91-6 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-[(methylsulfinyl)amino]propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 760958-93-8 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, 4-chloro-7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

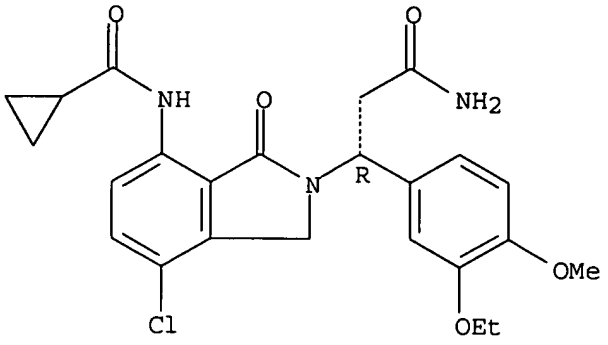
Absolute stereochemistry.



RN 760958-96-1 HCAPLUS
CN 2H-Isoindole-2-propanamide, 4-chloro-7-[(cyclopropylcarbonyl)amino]-β-

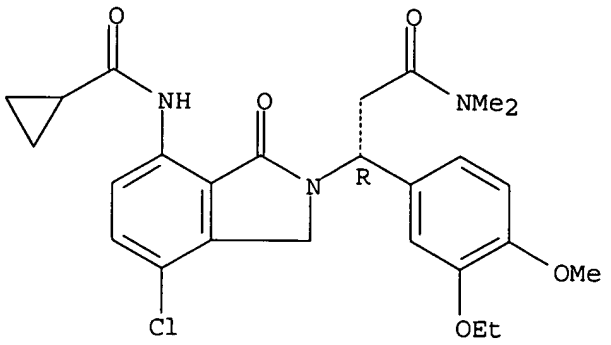
(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



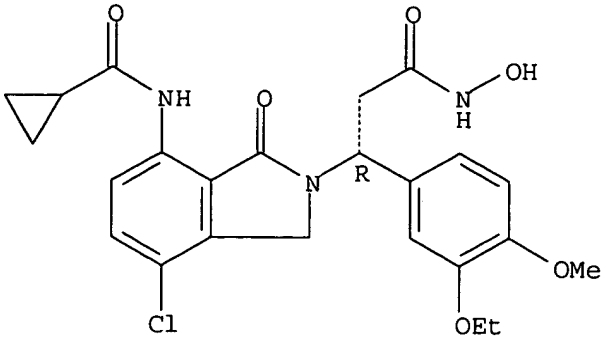
RN 760958-97-2 HCAPLUS
CN 2H-Isoindole-2-propanamide, 4-chloro-7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



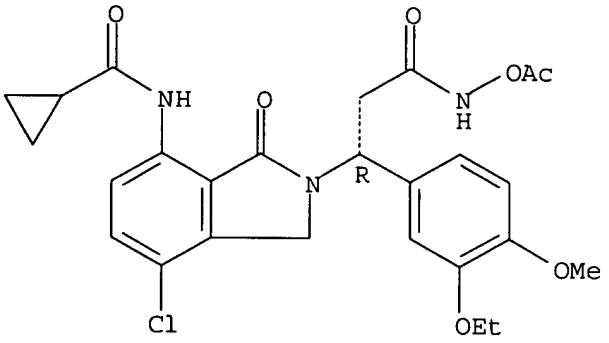
RN 760958-98-3 HCAPLUS
CN 2H-Isoindole-2-propanamide, 4-chloro-7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N-hydroxy-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



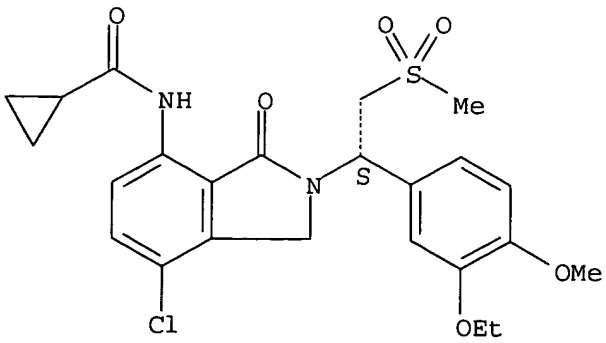
RN 760958-99-4 HCAPLUS
CN 2H-Isoindole-2-propanamide, N-(acetyloxy)-4-chloro-7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 760959-00-0 HCAPLUS
CN Cyclopropanecarboxamide, N-[7-chloro-2-[(1S)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

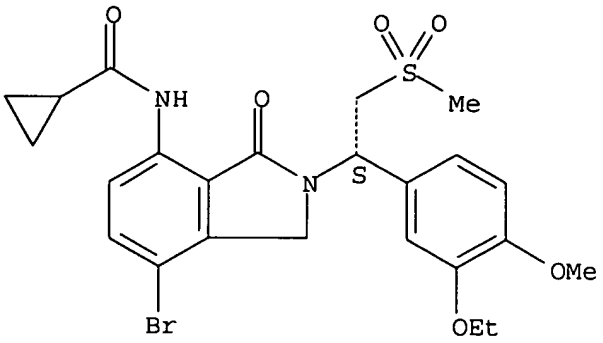
Absolute stereochemistry.



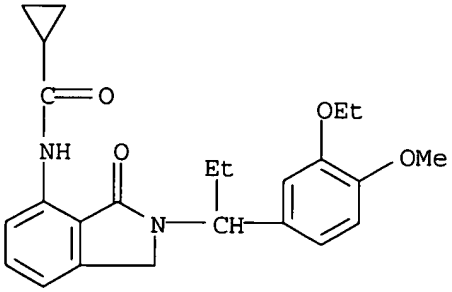
RN 760959-03-3 HCAPLUS
CN Cyclopropanecarboxamide, N-[7-bromo-2-[(1S)-1-(3-ethoxy-4-methoxyphenyl)-2-

(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

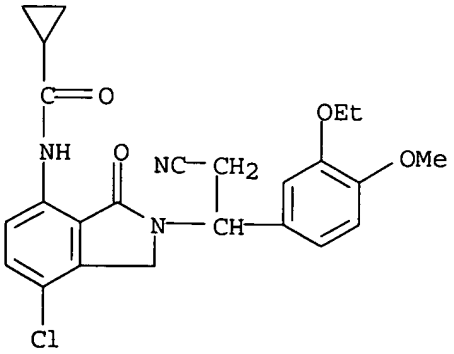
Absolute stereochemistry.



RN 760959-04-4 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

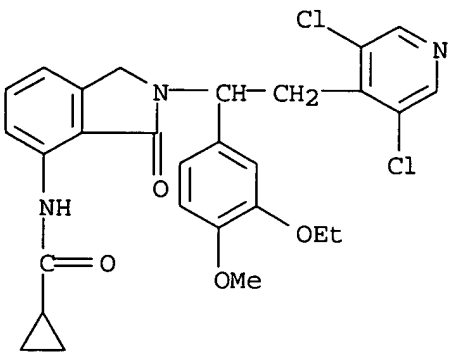


RN 760959-06-6 HCAPLUS
CN Cyclopropanecarboxamide, N-[7-chloro-2-[2-cyano-1-(3-ethoxy-4-methoxyphenyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)



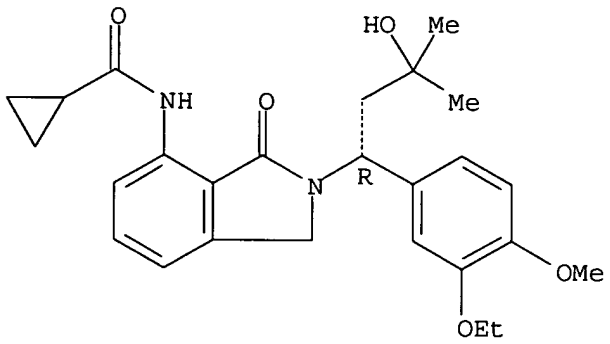
RN 760959-07-7 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[2-(3,5-dichloro-4-pyridinyl)-1-(3-ethoxy-4-methoxyphenyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX

NAME)



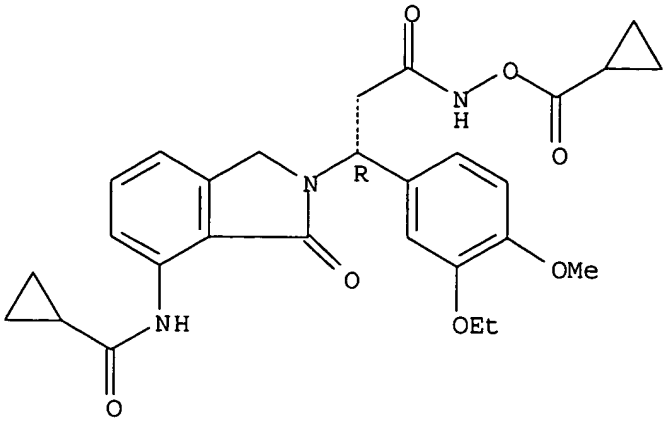
RN 760959-09-9 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-hydroxy-3-methylbutyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



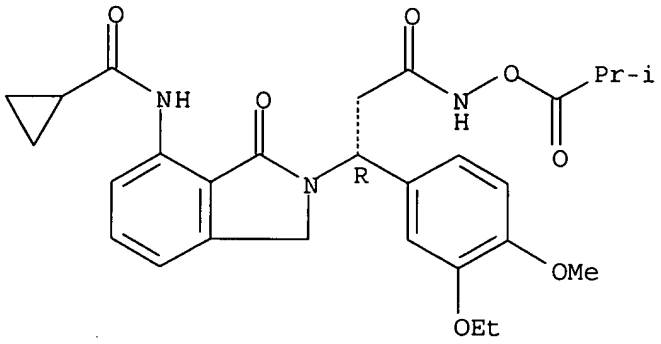
RN 760959-12-4 HCAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-N-[(cyclopropylcarbonyl)oxy]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



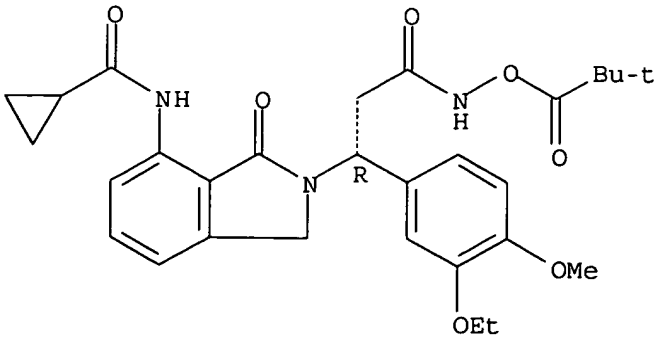
RN 760959-13-5 HCAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N-(2-methyl-1-oxopropoxy)-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



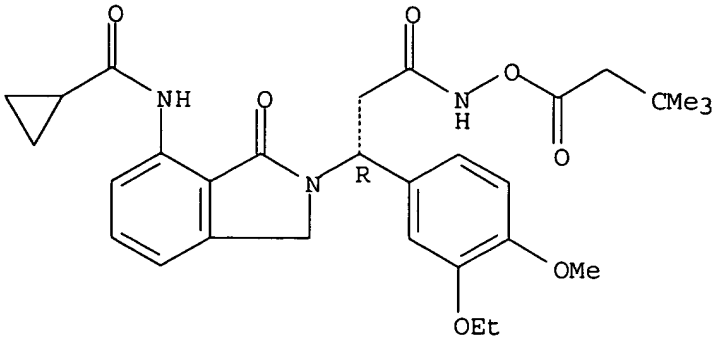
RN 760959-14-6 HCAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-N-(2,2-dimethyl-1-oxopropoxy)-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



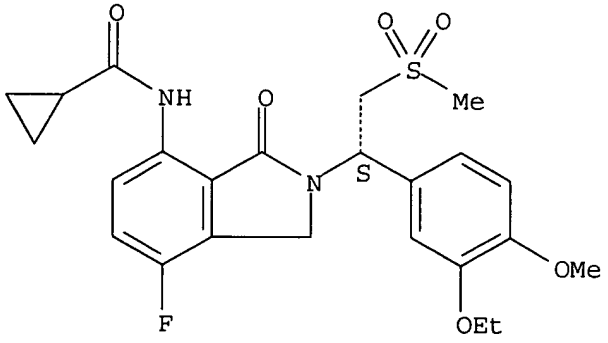
RN 760959-15-7 HCAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-N-(3,3-dimethyl-1-oxobutoxy)-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



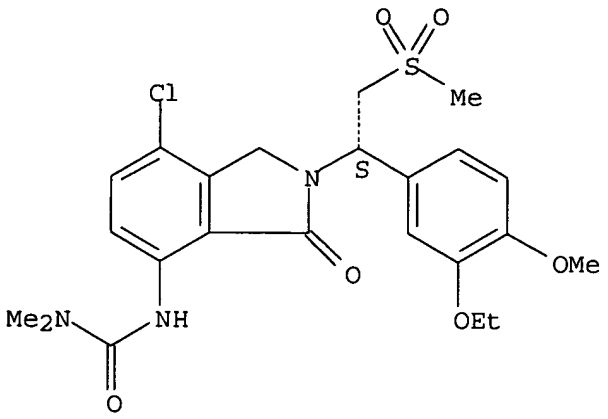
RN 760959-16-8 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1S)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-7-fluoro-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



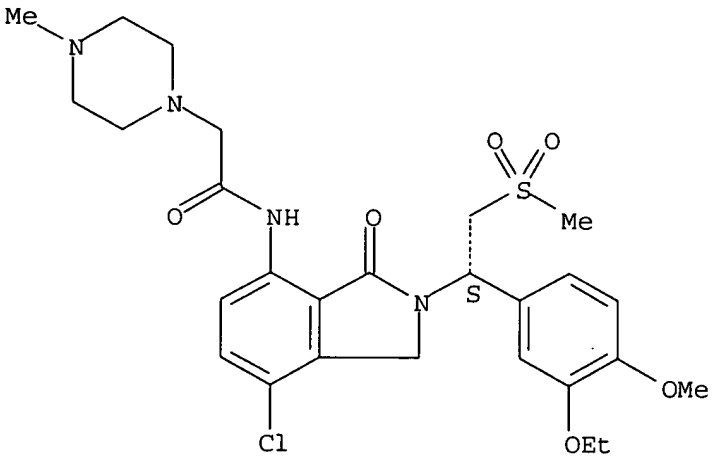
RN 760959-18-0 HCAPLUS
CN Urea, N'-[7-chloro-2-[(1S)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]-N,N-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



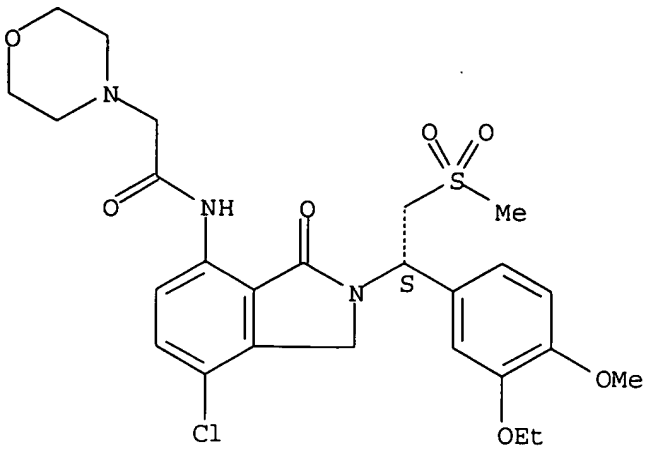
RN 760959-20-4 HCAPLUS
CN 1-Piperazineacetamide, N-[7-chloro-2-[(1S)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]-4-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 760959-22-6 HCAPLUS
CN 4-Morpholineacetamide, N-[7-chloro-2-[(1S)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]-, monohydrochloride (9CI) (CA INDEX NAME)

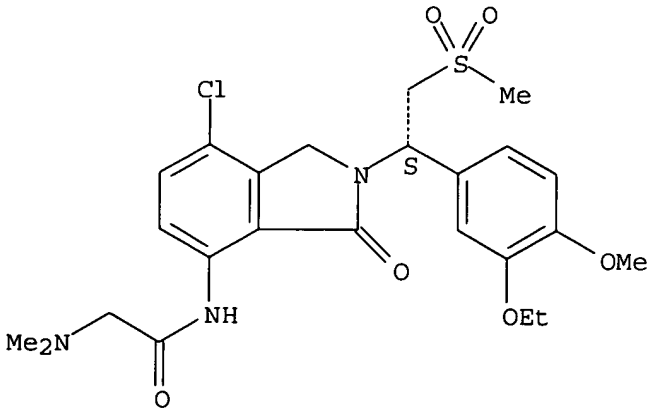
Absolute stereochemistry.



● HCl

RN 760959-23-7 HCAPLUS
CN Acetamide, N-[7-chloro-2-[(1S)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]-2-(dimethylamino)-, monohydrochloride (9CI) (CA INDEX NAME)

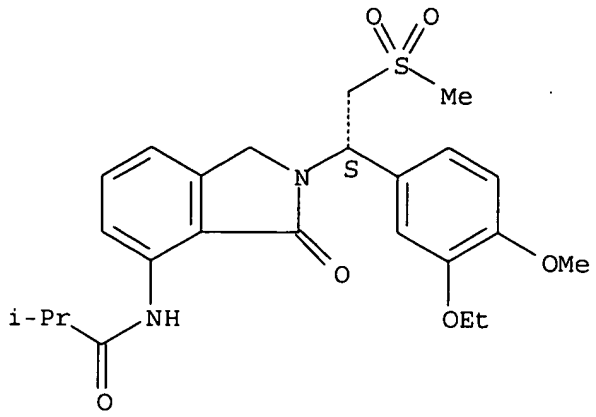
Absolute stereochemistry.



● HCl

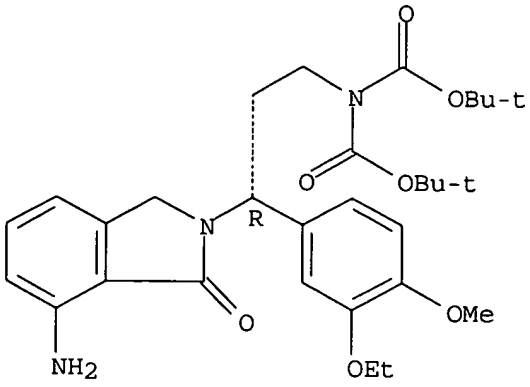
RN 760959-24-8 HCAPLUS
CN Propanamide, N-[2-[(1S)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



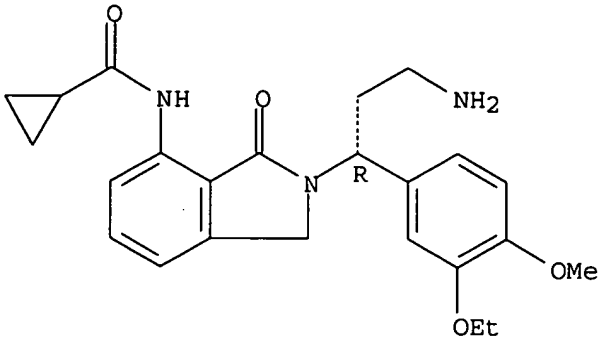
IT **760958-81-4 760958-84-7 760958-89-2**
760958-94-9 760959-05-5 760959-19-1
760959-21-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of aminoisoindolone derivs. via heterocyclization of aminopropanol derivs. and benzoic acid derivs.)
RN 760958-81-4 HCAPLUS
CN Imidodicarbonic acid, [(3R)-3-(7-amino-1,3-dihydro-1-oxo-2H-isoindol-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



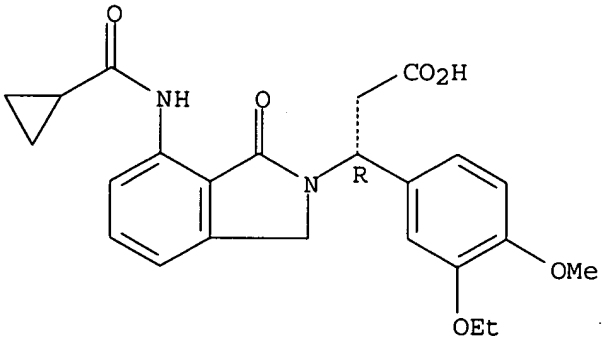
RN 760958-84-7 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-3-amino-1-(3-ethoxy-4-methoxyphenyl)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



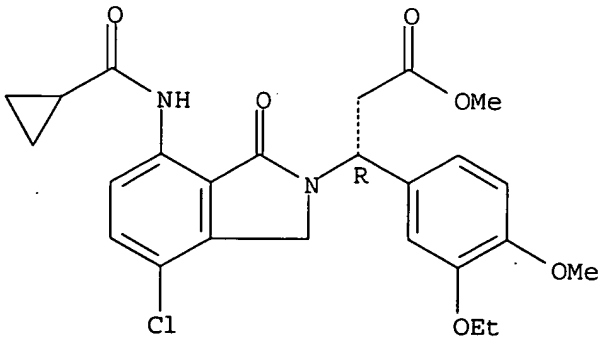
RN 760958-89-2 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, 7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



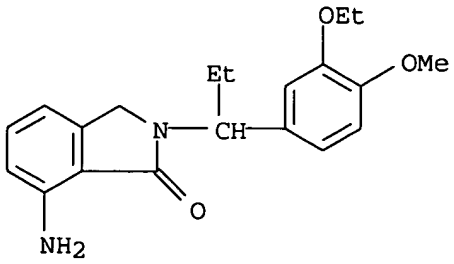
RN 760958-94-9 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, 4-chloro-7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, methyl ester, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



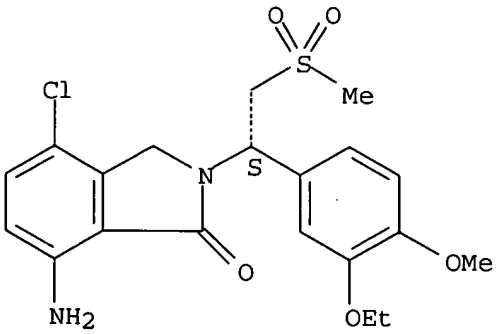
RN 760959-05-5 HCAPLUS
CN 1H-Isoindol-1-one, 7-amino-2-[1-(3-ethoxy-4-methoxyphenyl)propyl]-2,3-

dihydro- (9CI) (CA INDEX NAME)



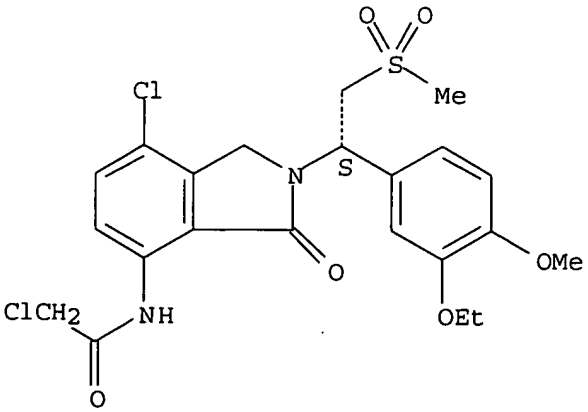
RN 760959-19-1 HCAPLUS
CN 1H-Isoindol-1-one, 7-amino-4-chloro-2-[(1S)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 760959-21-5 HCAPLUS
CN Acetamide, 2-chloro-N-[7-chloro-2-[(1S)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



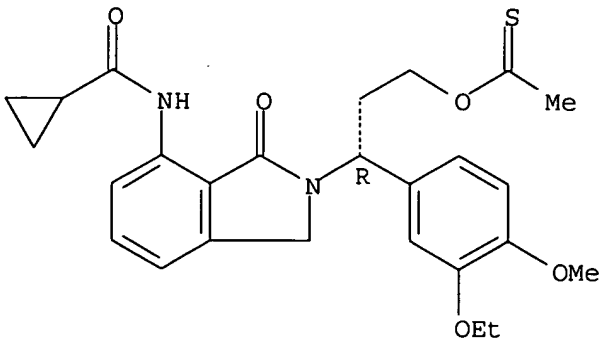
IT **760958-92-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(preparation of aminoisoindolone derivs. via heterocyclization of aminopropanol derivs. and benzoic acid derivs.)

RN 760958-92-7 HCAPLUS

CN Ethanethioic acid, O-[(3R)-3-[7-[(cyclopropylcarbonyl)amino]-1,3-dihydro-1-oxo-2H-isoindol-2-yl]-3-(3-ethoxy-4-methoxyphenyl)propyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L12 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:780509 HCAPLUS

DOCUMENT NUMBER: 141:295861

TITLE: A preparation of novel isoindolone derivatives, useful as **PDE4** inhibitors

INVENTOR(S): Man, Hon-Wah; Muller, George W.

PATENT ASSIGNEE(S): Celgene Corporation, USA

SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004080422	A2	20040923	WO 2004-US7742	20040312
WO 2004080422	A3	20041028		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2518513	AA	20040923	CA 2004-2518513	20040312
US 2004259873	A1	20041223	US 2004-798372	20040312
US 6911464	B2	20050628		
EP 1606256	A2	20051221	EP 2004-720480	20040312
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK

US 2005203090	A1	20050915	US 2005-124280	20050509
PRIORITY APPLN. INFO.:			US 2003-454149P	P 20030312
			US 2004-798372	A3 20040312
			WO 2004-US7742	W 20040312

OTHER SOURCE(S): MARPAT 141:295861
GI

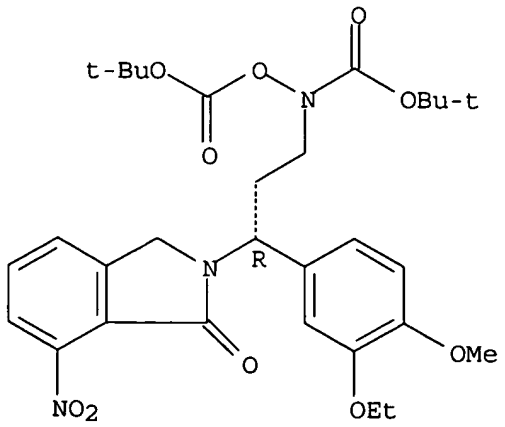
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to a preparation of novel isoindolone derivs. of formula I [wherein: Y is C(O), CH2, CH2C(O), or SO2; R1 and R2 are independently selected from (cyclo)alkyl, CF2H, CF3, or CH2CHF2, etc.; Z1 is H, alkyl, NH2, or NH2, etc.; Z2 is H or CHO, -C(O)-alkyl, or -C(O)Ph, etc.; X1, X2, X3, and X4 are independently selected from H, halogen, NO2, CF3, alkyl, or alkylimidazolyl, etc.; R3 and R4 are independently H or alkyl], useful for treatment or prevention of various diseases and disorders, for example, diseases associated with **PDE4** (no biol. data). For instance, isoindolone derivative II was prepared via amination of N-(hydroxypropyl)isoindolone derivative III by N,O-(tert-butoxycarbonyl)hydroxylamine with a yield of 78%.

IT **761434-15-5P 761434-16-6P 761434-20-2P**
761434-23-5P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of novel isoindolone derivs. useful as **PDE4** inhibitors)

RN 761434-15-5 HCAPLUS
CN Carbamic acid, [(3R)-3-(1,3-dihydro-7-nitro-1-oxo-2H-isoindol-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propyl][[(1,1-dimethylethoxy)carbonyl]oxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

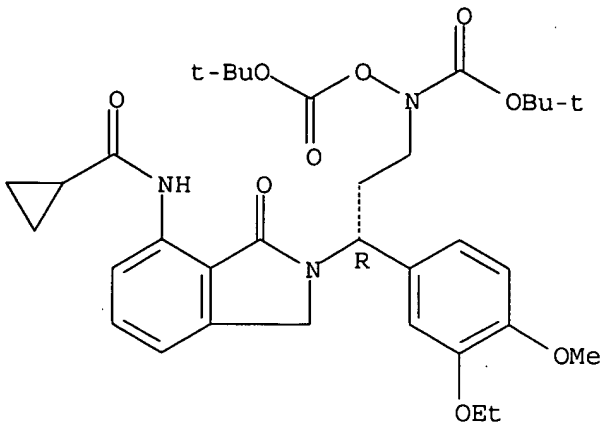
Absolute stereochemistry.



RN 761434-16-6 HCAPLUS
CN Carbamic acid, [(3R)-3-[7-[(cyclopropylcarbonyl)amino]-1,3-dihydro-1-oxo-2H-isoindol-2-yl]-3-(3-ethoxy-4-methoxyphenyl)propyl][[(1,1-dimethylethoxy)carbonyl]oxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX

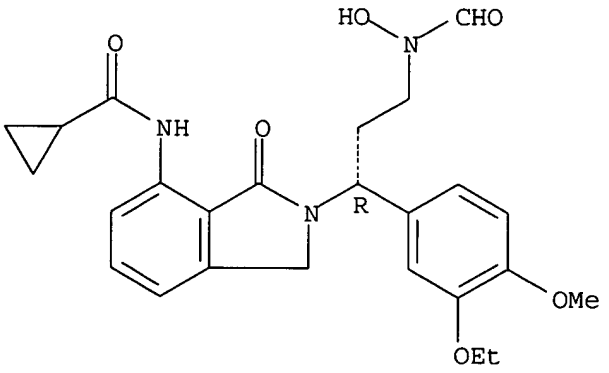
NAME)

Absolute stereochemistry.



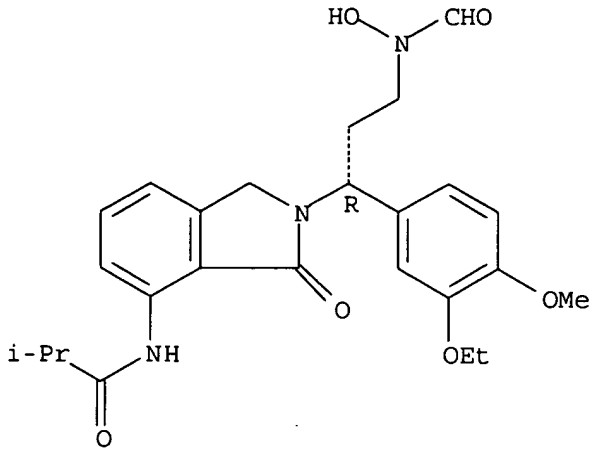
RN 761434-20-2 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-(formylhydroxyamino)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



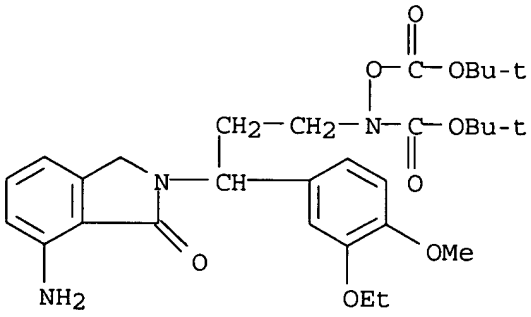
RN 761434-23-5 HCAPLUS
CN Propanamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-(formylhydroxyamino)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



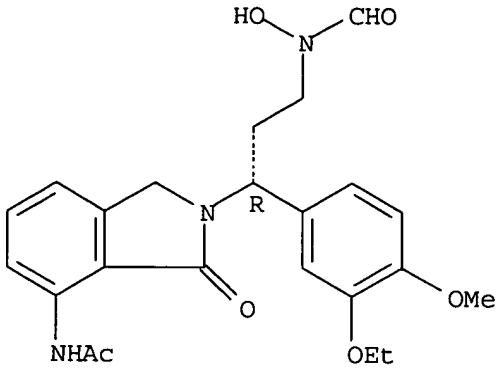
IT **761434-18-8P 761434-21-3P 761434-27-9P**
761434-28-0P 761434-29-1P 761434-30-4P
761434-32-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel isoindolone derivs. useful as **PDE4** inhibitors)

RN 761434-18-8 HCAPLUS
CN Carbamic acid, [3-(7-amino-1,3-dihydro-1-oxo-2H-isoindol-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propyl][[(1,1-dimethylethoxy)carbonyl]oxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



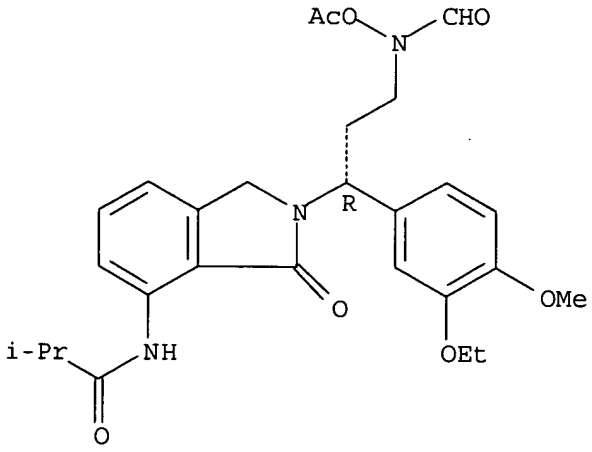
RN 761434-21-3 HCAPLUS
CN Acetamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-(formylhydroxyamino)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



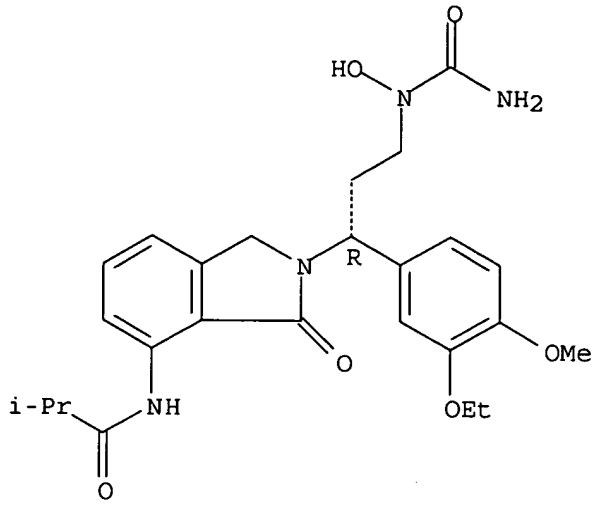
RN 761434-27-9 HCAPLUS
CN Propanamide, N-[2-[(1R)-3-[(acetyloxy)formylamino]-1-(3-ethoxy-4-methoxyphenyl)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



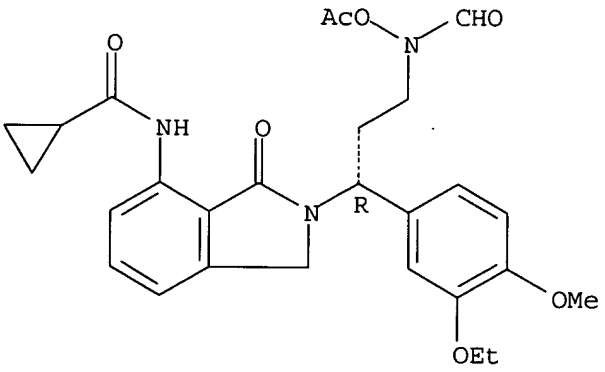
RN 761434-28-0 HCAPLUS
CN Propanamide, N-[2-[(1R)-3-[(aminocarbonyl)hydroxyamino]-1-(3-ethoxy-4-methoxyphenyl)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

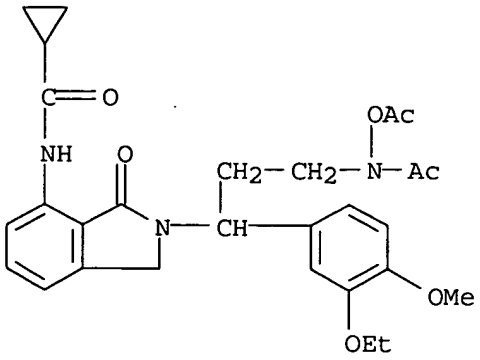


RN 761434-29-1 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-3-[(acetyloxy)formylamino]-1-(3-ethoxy-4-methoxyphenyl)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

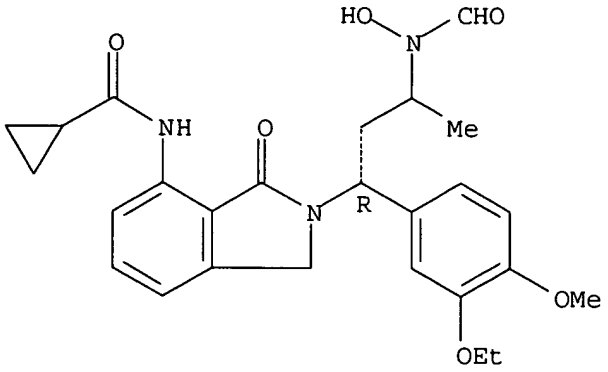


RN 761434-30-4 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[3-[acetyl(acetyloxy)amino]-1-(3-ethoxy-4-methoxyphenyl)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)



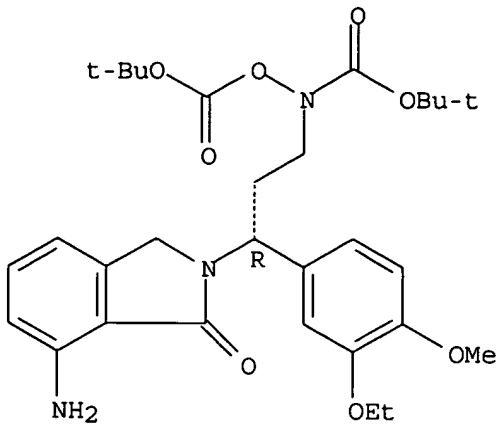
RN 761434-32-6 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-(formylhydroxyamino)butyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

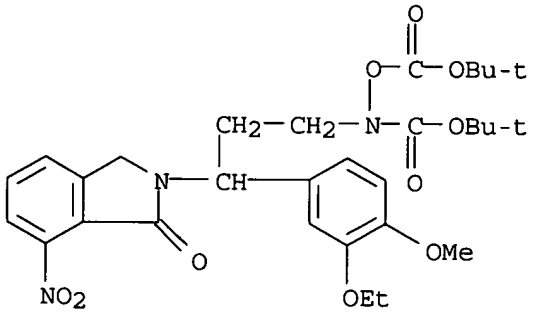


IT **761434-17-7 761434-19-9 761434-22-4**
761434-24-6 761434-31-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of novel isoindolone derivs. useful as **PDE4** inhibitors)
RN 761434-17-7 HCAPLUS
CN Carbamic acid, [(3R)-3-(7-amino-1,3-dihydro-1-oxo-2H-isoindol-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propyl][[(1,1-dimethylethoxy)carbonyl]oxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

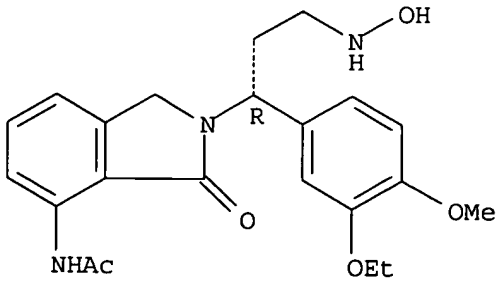


RN 761434-19-9 HCAPLUS
CN Carbamic acid, [3-(1,3-dihydro-7-nitro-1-oxo-2H-isoindol-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propyl][[(1,1-dimethylethoxy)carbonyl]oxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



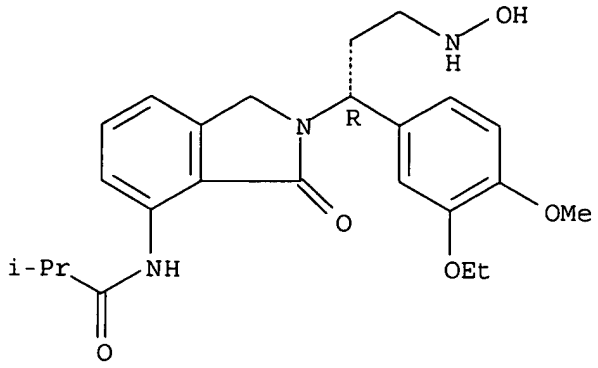
RN 761434-22-4 HCAPLUS
CN Acetamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-(hydroxyamino)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

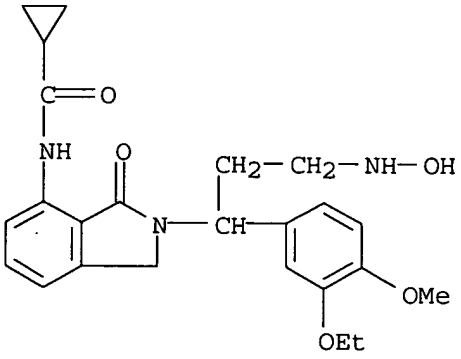


RN 761434-24-6 HCAPLUS
CN Propanamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-(hydroxyamino)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

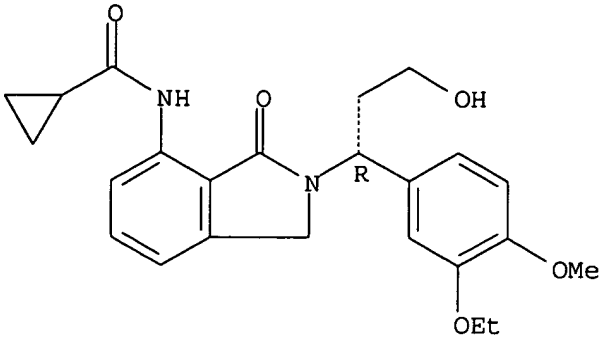


RN 761434-31-5 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)-3-(hydroxyamino)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)



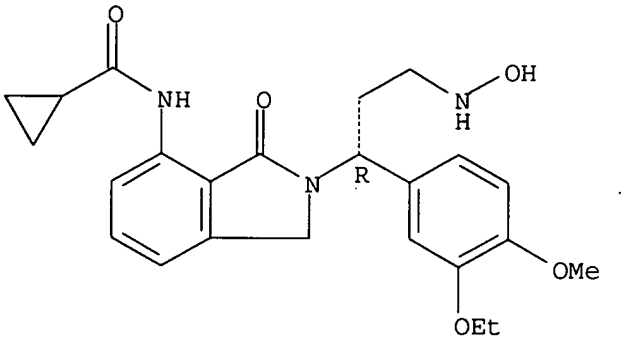
IT **760958-78-9P 760958-82-5P 761434-14-4P 761434-34-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of novel isoindolone derivs. useful as **PDE4** inhibitors)
RN 760958-78-9 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-hydroxypropyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



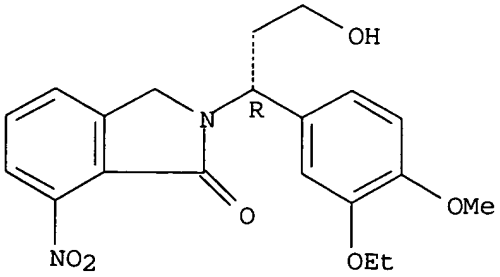
RN 760958-82-5 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-(hydroxyamino)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



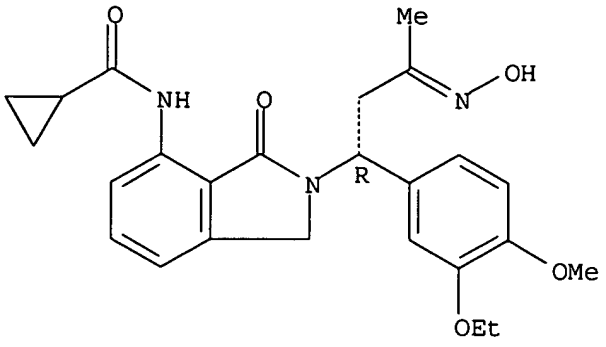
RN 761434-14-4 HCAPLUS
CN 1H-Isoindol-1-one, 2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-hydroxypropyl]-2,3-dihydro-7-nitro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 761434-34-8 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-(hydroxyimino)butyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



L12 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:589381 HCAPLUS
DOCUMENT NUMBER: 141:140314
TITLE: Preparation of 2-(fluoroalkoxyphenylalkyl)-1,3-dihydroisoindolones as **PDE4**, TNF-α, and/or MMP inhibitors
INVENTOR(S): Muller, George W.; Man, Hon-Wah; Zhang, Weihong
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004060313	A2	20040722	WO 2003-US41568	20031229
WO 2004060313	A3	20050915		
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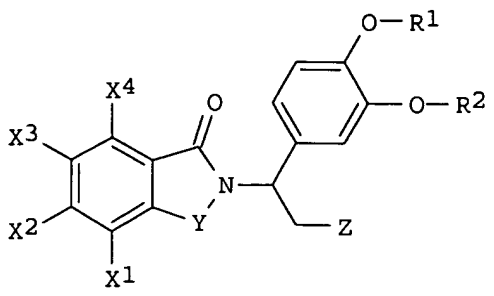
US 2004204448	A1	20041014	US 2003-748085	20031229
EP 1587474	A2	20051026	EP 2003-808605	20031229
EP 1587474	A3	20051102		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: US 2002-436975P P 20021230
WO 2003-US41568 W 20031229

OTHER SOURCE(S): MARPAT 141:140314
GI



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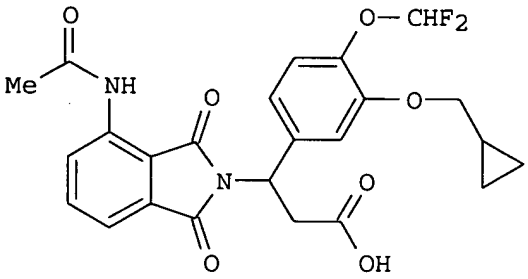


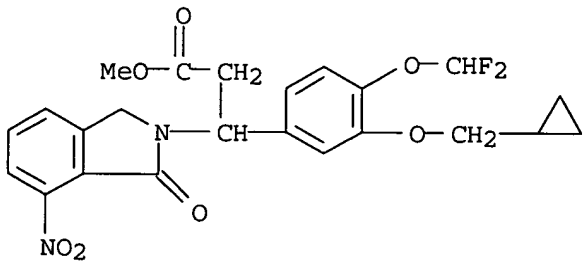
II

AB Title compds. I [wherein X1-X4 = independently H, halo, NO2, NH2, CF3, alkyl, cycloalkyl(alkyl), NR7R8-(alkyl), R8CONH-(alkyl), NR7R8CONH-(alkyl), R8OCONH-(alkyl), R8O-(alkyl), imidazolyl(alkyl), pyrrolyl(alkyl), oxadiazolyl(alkyl), triazolyl(alkyl); or X1 and X2 or X2 and X3 or X3 and X4 may be taken together to form a (hetero)cycloalkyl ring; Y = CO, CH2, CH2CO, COCH2, SO2; Z = H, COR3, alkylsulfonyl(alkyl), alkyl, CH2OH, alkoxymethyl, CN; R1 and R2 = independently CHF2, alkyl, cycloalkyl(alkyl); at least one of R1 and R2 = CHF2; R3 = NR4R5, alkyl, OH, alkoxy, (un)substituted Ph, PhCH2; R4 and R5 = independently H, alkyl, OH, OCOR6; R6 = alkyl(amino), Ph, PhCH2, aryl; R7 and R8 = independently H, alkyl, cycloalkyl(alkyl), NR7R8-alkyl, R8O-alkyl, Ph, PhCH2, aryl; or pharmaceutically acceptable salts, hydrates, solvates, clathrates, stereoisomers, and prodrugs thereof] were prepared For example, alkylation of 3,4-dihydroxybenzaldehyde with chlorodifluoromethane in the presence of K2CO3 in DMF gave 4-difluoromethoxy-3-hydroxybenzaldehyde (15%), which was further alkylated with bromomethylcyclopropane under the same conditions to afford 3-cyclopropylmethoxy-4-difluoromethoxybenzaldehyde (100%). Reaction of the benzaldehyde with ammonium acetate in 95% EtOH, followed by addition of malonic acid provided 3-amino-3-(3-cyclopropylmethoxy-4-difluoromethoxyphenyl)propionic acid (52%). Condensation of the amine with 3-acetamidophthalic anhydride using sodium acetate in AcOH yielded the isoindoledione II (85%). I and their pharmaceutical compns., optionally in combination with another therapeutic agent, are useful for the treatment or prevention of diseases associated with phosphodiesterase 4 (**PDE4**) inhibition, abnormal tumor necrosis factor α (TNF-α) levels , and/or matrix metalloproteinase (MMP) inhibition, such as myelodysplastic syndrome, myeloproliferative disease, complex regional pain syndrome, cancer, inflammatory diseases, and autoimmune diseases (no data).

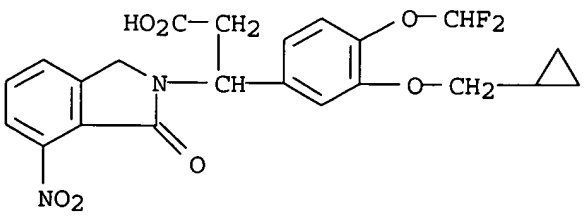
IT **725256-76-8P**, 3-[3-(Cyclopropylmethoxy)-4-difluoromethoxyphenyl]-3-(7-nitro-1-oxo-1,3-dihydroisoindol-2-yl)propionic acid methyl ester
725256-77-9P, 3-[3-(Cyclopropylmethoxy)-4-difluoromethoxyphenyl]-3-(7-nitro-1-oxo-1,3-dihydroisoindol-2-yl)propionic acid

725256-78-0P, 3-[3-(Cyclopropylmethoxy)-4-difluoromethoxyphenyl]-3-(7-nitro-1-oxo-1,3-dihydroisoindol-2-yl)-N,N-dimethylpropionamide **725256-83-7P**, 3-[7-(Cyclopropylcarbonylamino)-1-oxo-1,3-dihydroisoindol-2-yl]-3-(4-difluoromethoxy-3-ethoxyphenyl)propionic acid methyl ester **725256-84-8P**, 3-(7-Amino-1-oxo-1,3-dihydroisoindol-2-yl)-3-(4-difluoromethoxy-3-ethoxyphenyl)propionic acid methyl ester **725256-85-9P**, 3-(7-Acetylamino-1-oxo-1,3-dihydroisoindol-2-yl)-3-(4-difluoromethoxy-3-ethoxyphenyl)propionic acid methyl ester **725256-86-0P**, 3-[7-(Acetylamino)-1-oxo-1,3-dihydroisoindol-2-yl]-3-(4-difluoromethoxy-3-ethoxyphenyl)propionic acid **725256-87-1P**, 3-[7-(Cyclopropylcarbonylamino)-1-oxo-1,3-dihydroisoindol-2-yl]-3-(4-difluoromethoxy-3-ethoxyphenyl)propionic acid **725257-12-5P**, 3-[3,4-Bis(difluoromethoxy)phenyl]-3-[7-(cyclopropylcarbonylamino)-1-oxo-1,3-dihydroisoindol-2-yl]propionic acid
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(**PDE4**, TNF-α, and/or MMP inhibitor; preparation of (fluoroalkoxyphenylalkyl)isoindolones as **PDE4**, TNF-α, and/or MMP inhibitors for treatment of inflammatory diseases, autoimmune diseases, cancer, and pain)

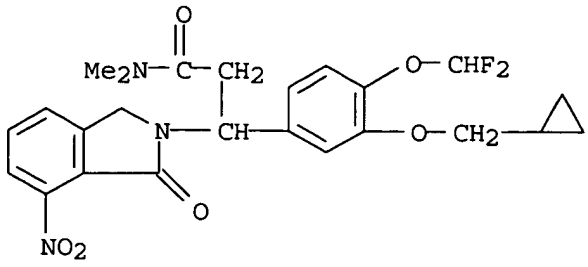
RN 725256-76-8 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-[3-(cyclopropylmethoxy)-4-(difluoromethoxy)phenyl]-1,3-dihydro-7-nitro-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



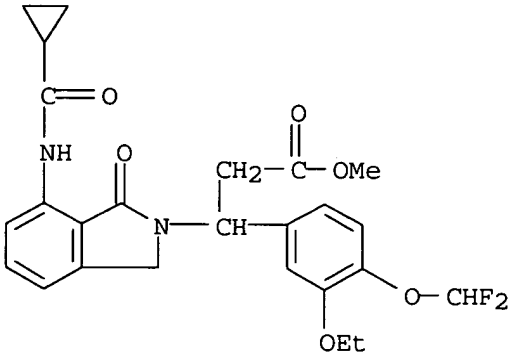
RN 725256-77-9 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-[3-(cyclopropylmethoxy)-4-(difluoromethoxy)phenyl]-1,3-dihydro-7-nitro-1-oxo- (9CI) (CA INDEX NAME)



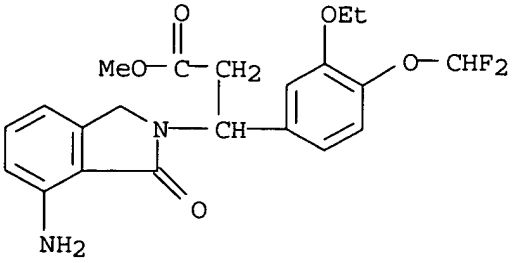
RN 725256-78-0 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-[3-(cyclopropylmethoxy)-4-(difluoromethoxy)phenyl]-1,3-dihydro-N,N-dimethyl-7-nitro-1-oxo- (9CI) (CA INDEX NAME)



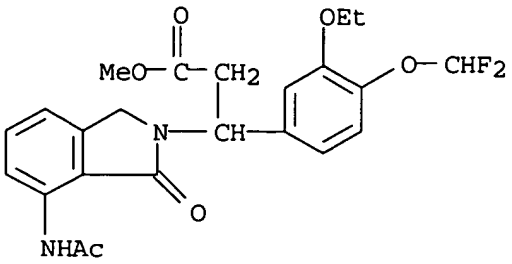
RN 725256-83-7 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, 7-[(cyclopropylcarbonyl)amino]-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



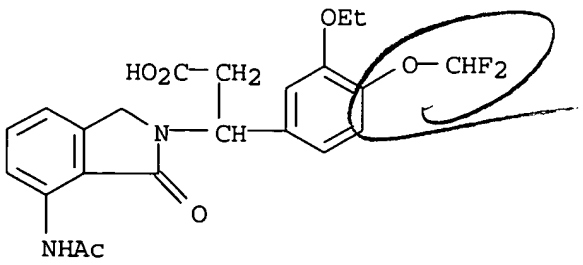
RN 725256-84-8 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, 7-amino-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



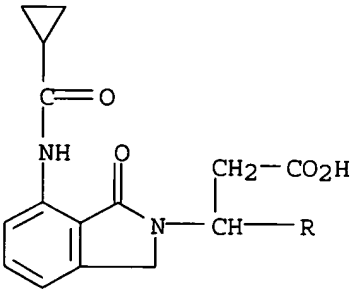
RN 725256-85-9 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, 7-(acetylamino)-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-1-oxo-, methyl ester (9CI) (CA INDEX NAME)

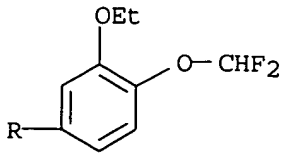


RN 725256-86-0 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, 7-(acetylamino)-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)

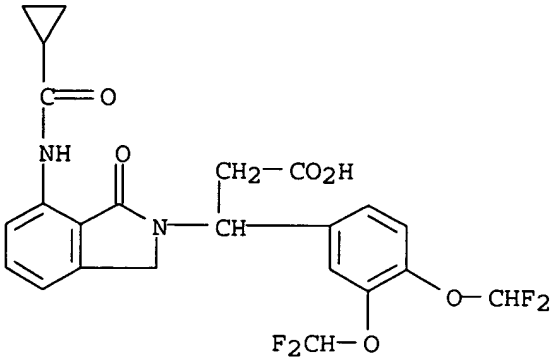


RN 725256-87-1 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, 7-[(cyclopropylcarbonyl)amino]-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)





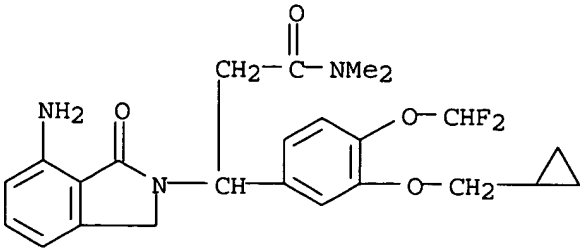
RN 725257-12-5 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-[3,4-bis(difluoromethoxy)phenyl]-7-[(cyclopropylcarbonyl)amino]-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



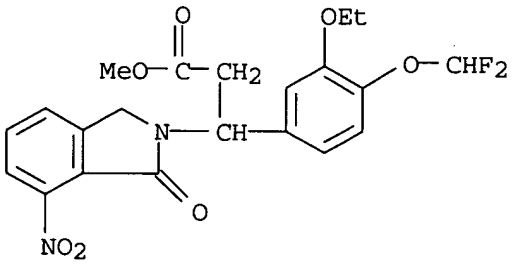
IT **725256-79-1P**, 3-(7-Amino-1-oxo-1,3-dihydroisoindol-2-yl)-3-[3-(cyclopropylmethoxy)-4-difluoromethoxyphenyl]-N,N-dimethylpropionamide **725256-82-6P**, 3-(4-Difluoromethoxy-3-ethoxyphenyl)-3-(7-nitro-1-oxo-1,3-dihydroisoindol-2-yl)propionic acid methyl ester **725256-88-2P**, Cyclopropanecarboxylic acid N-[2-[2-carbamoyl-1-(4-difluoromethoxy-3-ethoxyphenyl)ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl]amide **725256-89-3P**, Cyclopropanecarboxylic acid N-[2-[1-(4-difluoromethoxy-3-ethoxyphenyl)-2-(dimethylcarbamoyl)ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl]amide **725256-90-6P**, Cyclopropanecarboxylic acid N-[2-[1-(4-difluoromethoxy-3-ethoxyphenyl)-2-hydroxycarbamoylethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl]amide **725256-91-7P**, 3-(7-Acetylamino-1-oxo-1,3-dihydroisoindol-2-yl)-3-(4-difluoromethoxy-3-ethoxyphenyl)propionamide **725256-92-8P**, 3-(7-Acetylamino-1-oxo-1,3-dihydroisoindol-2-yl)-3-(4-difluoromethoxy-3-ethoxyphenyl)-N,N-dimethylpropionamide **725256-93-9P**, 3-(7-Acetylamino-1-oxo-1,3-dihydroisoindol-2-yl)-3-(4-difluoromethoxy-3-ethoxyphenyl)-N-hydroxypropionamide **725256-99-5P**, Cyclopropanecarboxylic acid N-[2-[1-(4-difluoromethoxy-3-ethoxyphenyl)-2-(methanesulfonyl)ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl]amide **725257-02-3P**, Cyclopropanecarboxylic acid N-[2-[2-carbamoyl-1-(4-difluoromethoxy-3-ethoxyphenyl)ethyl]-7-chloro-3-oxo-2,3-dihydro-1H-isoindol-4-yl]amide **725257-05-6P**, N-[2-[1-(4-Difluoromethoxy-3-ethoxyphenyl)-3-(morpholin-4-yl)-3-oxopropyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl]acetamide **725257-08-9P**, 3-[3,4-Bis(difluoromethoxy)phenyl]-3-[4-chloro-7-(cyclopropylcarbonylamino)-1-oxo-1,3-dihydroisoindol-2-yl]propionic acid methyl ester **725257-11-4P**, Cyclopropanecarboxylic acid N-[2-[1-[3,4-bis(difluoromethoxy)phenyl]-2-(dimethylcarbamoyl)ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl]amide **725257-13-6P**, Cyclopropanecarboxylic acid N-[2-[1-[3,4-bis(difluoromethoxy)phenyl]-2-carbamoylethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl]amide **725257-14-7P**, Cyclopropanecarboxylic acid N-[2-[1-[3,4-bis(difluoromethoxy)phenyl]-2-hydroxycarbamoylethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl]amide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**PDE4**, TNF-α, and/or MMP inhibitor; preparation of (fluoroalkoxyphenylalkyl)isoindolones as **PDE4**, TNF-α, and/or MMP inhibitors for treatment of inflammatory diseases, autoimmune diseases, cancer, and pain)

RN 725256-79-1 HCAPLUS

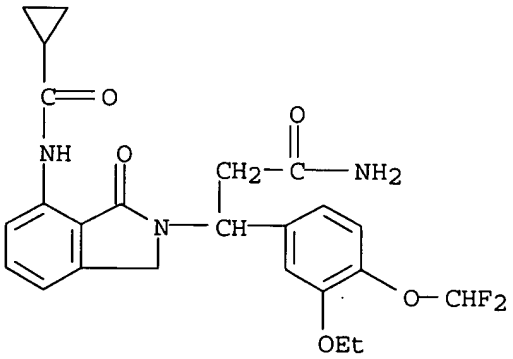
CN 2H-Isoindole-2-propanamide, 7-amino-β-[3-(cyclopropylmethoxy)-4-(difluoromethoxy)phenyl]-1,3-dihydro-N,N-dimethyl-1-oxo- (9CI) (CA INDEX NAME)



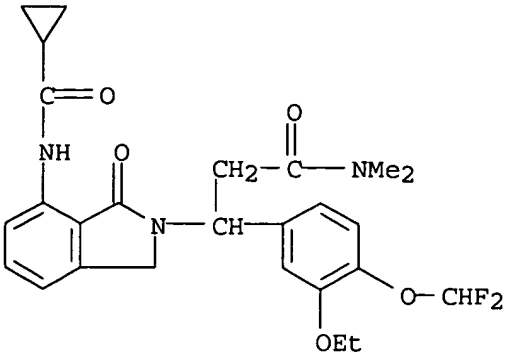
RN 725256-82-6 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-7-nitro-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



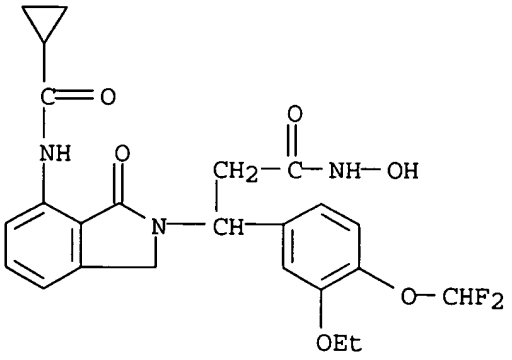
RN 725256-88-2 HCAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



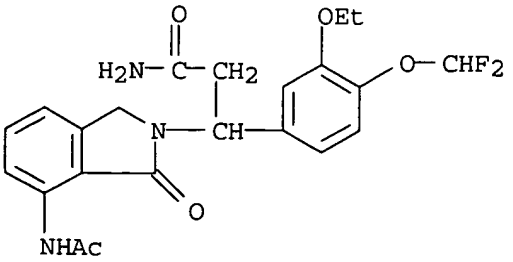
RN 725256-89-3 HCAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-N,N-dimethyl-1-oxo- (9CI) (CA INDEX NAME)



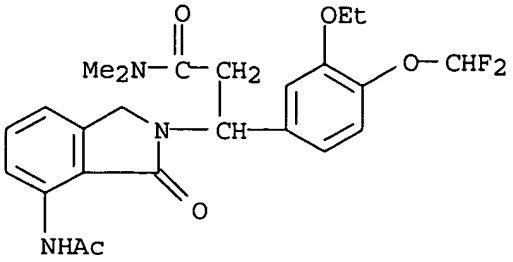
RN 725256-90-6 HCAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-N-hydroxy-1-oxo- (9CI) (CA INDEX NAME)



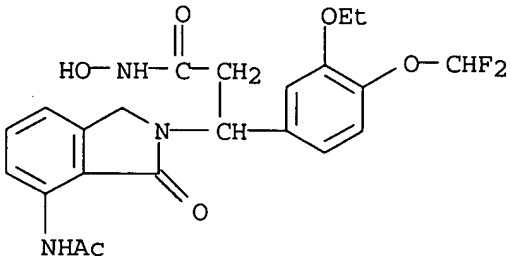
RN 725256-91-7 HCAPLUS
CN 2H-Isoindole-2-propanamide, 7-(acetylamino)-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



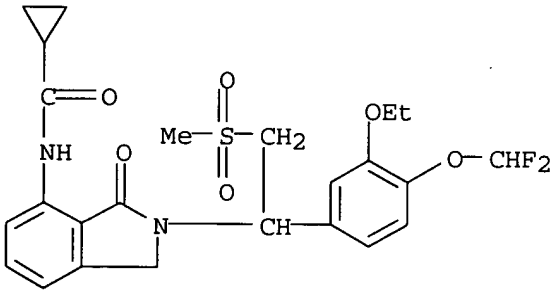
RN 725256-92-8 HCAPLUS
CN 2H-Isoindole-2-propanamide, 7-(acetylamino)-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-N,N-dimethyl-1-oxo- (9CI) (CA INDEX NAME)



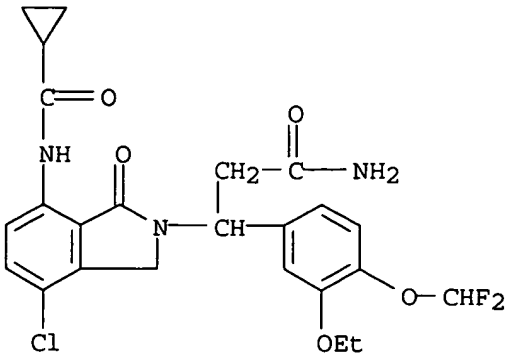
RN 725256-93-9 HCAPLUS
CN 2H-Isoindole-2-propanamide, 7-(acetylamino)-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-N-hydroxy-1-oxo- (9CI) (CA INDEX NAME)



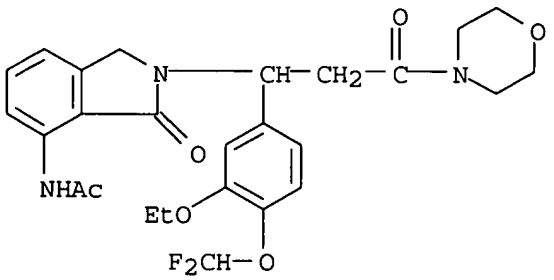
RN 725256-99-5 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[1-[4-(difluoromethoxy)-3-ethoxyphenyl]-2-(methylsulfonyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)



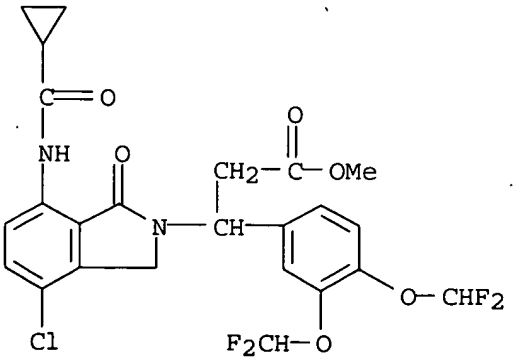
RN 725257-02-3 HCAPLUS
CN 2H-Isoindole-2-propanamide, 4-chloro-7-[(cyclopropylcarbonyl)amino]-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



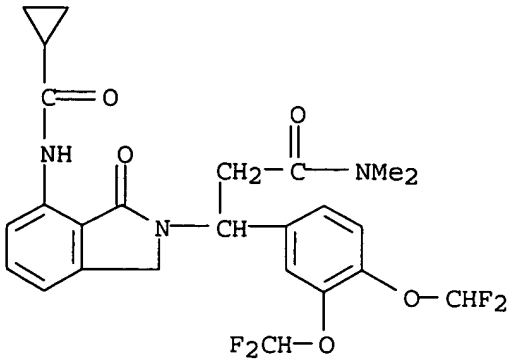
RN 725257-05-6 HCAPLUS
CN Acetamide, N-[2-[1-[4-(difluoromethoxy)-3-ethoxyphenyl]-3-(4-morpholinyl)-3-oxopropyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)



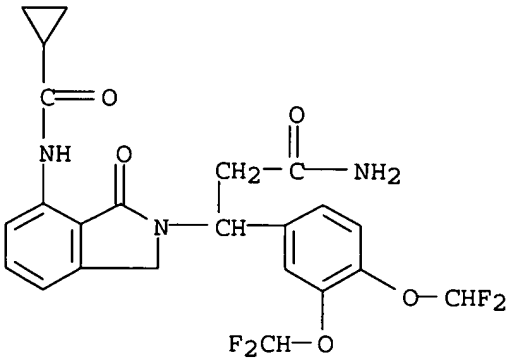
RN 725257-08-9 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-[3,4-bis(difluoromethoxy)phenyl]-4-chloro-7-[(cyclopropylcarbonyl)amino]-1,3-dihydro-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



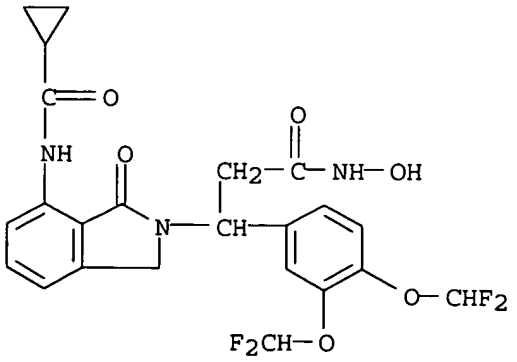
RN 725257-11-4 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-[3,4-bis(difluoromethoxy)phenyl]-7-[(cyclopropylcarbonyl)amino]-1,3-dihydro-N,N-dimethyl-1-oxo- (9CI) (CA INDEX NAME)



RN 725257-13-6 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-[3,4-bis(difluoromethoxy)phenyl]-7-[(cyclopropylcarbonyl)amino]-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



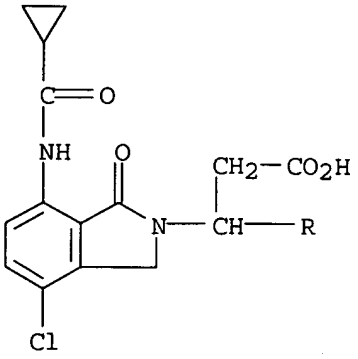
RN 725257-14-7 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-[3,4-bis(difluoromethoxy)phenyl]-7-[(cyclopropylcarbonyl)amino]-1,3-dihydro-N-hydroxy-1-oxo- (9CI) (CA INDEX NAME)

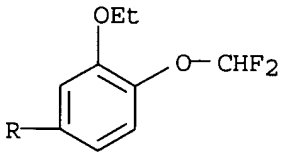


IT **725257-03-4**, 3-[4-Chloro-7-(cyclopropylcarbonylamino)-1-oxo-1,3-dihydroisoindol-2-yl]-3-(4-difluoromethoxy-3-ethoxyphenyl)propionic acid
725257-15-8, 3-[3,4-Bis(difluoromethoxy)phenyl]-3-[7-

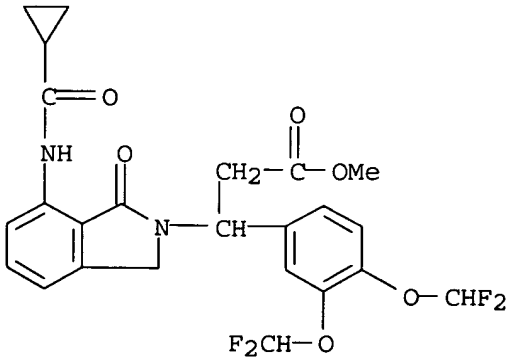
(cyclopropylcarbonylamino)-1-oxo-1,3-dihydroisoindol-2-yl]propionic acid methyl ester
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of (fluoroalkoxyphenylalkyl)isoindolones as **PDE4**, TNF-α, and/or MMP inhibitors for treatment of inflammatory diseases, autoimmune diseases, cancer, and pain)

RN 725257-03-4 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, 4-chloro-7-[(cyclopropylcarbonyl)amino]-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)





RN 725257-15-8 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-[3,4-bis(difluoromethoxy)phenyl]-7-[(cyclopropylcarbonyl)amino]-1,3-dihydro-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



L12 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:531300 HCAPLUS
DOCUMENT NUMBER: 141:94292

TITLE: Methods of using and compositions comprising (-)-3-(3,4-dimethoxy-phenyl)-3-(1-oxo-1,3-dihydro-isoindol-2-yl)-propionamide

INVENTOR(S): Muller, George W.; Chen, Roger Shen-chu
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2

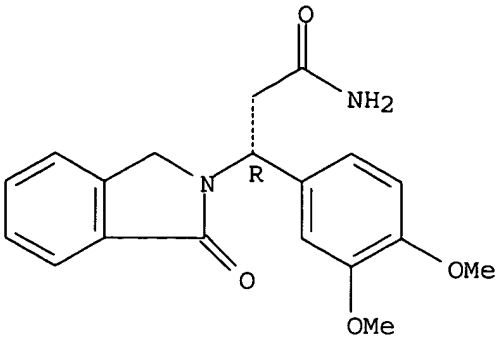
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004054501	A2	20040701	WO 2003-US36741	20031117
WO 2004054501	A3	20040826		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2506442	AA	20040701	CA 2003-2506442	20031117
US 2004167199	A1	20040826	US 2003-715184	20031117
EP 1569599	A2	20050907	EP 2003-789795	20031117
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003016256	A	20051004	BR 2003-16256	20031117
CN 1738614	A	20060222	CN 2003-80108901	20031117
PRIORITY APPLN. INFO.:			US 2002-427380P P	20021118
			WO 2003-US36741 W	20031117

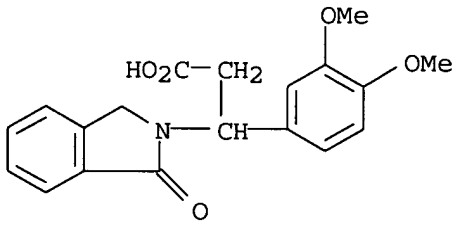
AB Enantiomerically pure (-)-3-(3,4-dimethoxy-phenyl)-3-(1-oxo-1,3-dihydro-isoindol-2-yl)-propionamide (I), prodrugs, metabolites, polymorphs, salts, solvates, and clathrates thereof are described. Methods of treating and/or preventing various diseases and disorders, such as those ameliorated by the reduction of levels of TNF-α or the inhibition of phosphodiesterase 4 (**PDE4**), are also disclosed. For example, I gave an TNF-α IC50 of 3 μM and 16 μM in LPS- and IL1β-induced production of TNF-α, resp.,. Also, I showed selectivity for human **PDE4** with IC50 of 4.4 μM.

IT **682359-77-9P**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation, compns. and therapeutic uses of (dimethoxyphenyl)-(oxodihydroisoindolyl)propionamide enantiomer as inhibitor of TNFα and **PDE4**)
RN 682359-77-9 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

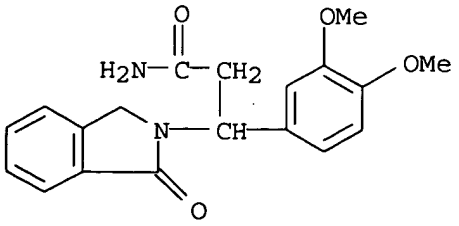
Absolute stereochemistry. Rotation (-).



IT **167886-75-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation, compns. and therapeutic uses of (dimethoxyphenyl)-(oxodihydroisoindolyl)propionamide enantiomer as inhibitor of TNFα and **PDE4**)
RN 167886-75-1 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)

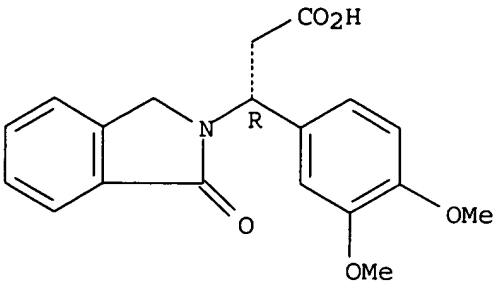


IT **167886-76-2P 713513-04-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, compns. and therapeutic uses of (dimethoxyphenyl)-(oxodihydroisoindolyl)propionamide enantiomer as inhibitor of TNFα and **PDE4**)
RN 167886-76-2 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



RN 713513-04-3 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L12 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:453020 HCAPLUS
DOCUMENT NUMBER: 141:12309
TITLE: Compositions comprising (+)-3-(3,4-dimethoxyphenyl)-3-(1-oxo-1,3-dihydroisoindol-2-yl)propionamide
INVENTOR(S): Muller, George W.; Chen, Roger Shen-chu
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004045597	A1	20040603	WO 2003-US36740	20031117
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2506232	AA	20040603	CA 2003-2506232	20031117
AU 2003294311	A1	20040615	AU 2003-294311	20031117
BR 2003016259	A	20051004	BR 2003-16259	20031117
EP 1581205	A1	20051005	EP 2003-789794	20031117
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1738613	A	20060222	CN 2003-80108923	20031117

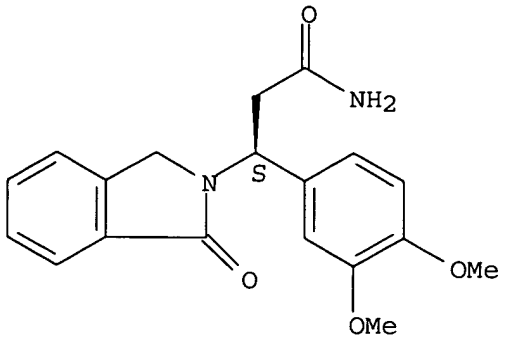
PRIORITY APPLN. INFO.: US 2002-427379P P 20021118
WO 2003-US36740 W 20031117

AB Enantiomerically pure (+)-3-(3,4-dimethoxyphenyl)-3-(1-oxo-1,3-dihydroisoindol-2-yl)propionamide (I), and prodrugs, metabolites, polymorphs, salts, solvates (e.g., hydrates), and clathrates are discussed. Methods of treating and/or preventing various diseases and disorders, such as those ameliorated by the reduction of levels of TNF-α or the inhibition of **PDE4**, are also disclosed. Thus, I was prepared in a series of steps starting from 3,4-dimethoxybenzaldehyde and

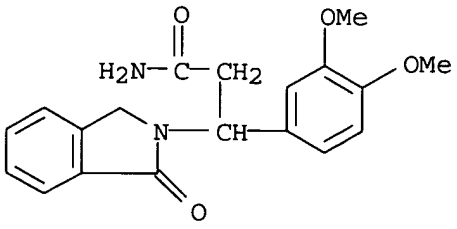
malonic acid. Capsules contained 40.0% I.

IT **682359-78-0P**
RL: PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(compns. comprising (dimethoxyphenyl)oxodihydroisoindolylpropionamide)
RN 682359-78-0 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo-, (βS)- (9CI) (CA INDEX NAME)

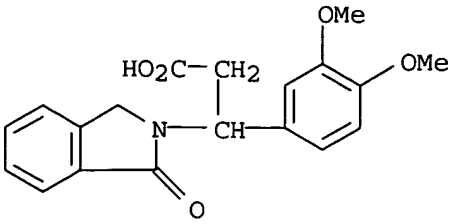
Absolute stereochemistry. Rotation (+).



IT **167886-76-2P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(compns. comprising (dimethoxyphenyl)oxodihydroisoindolylpropionamide)
RN 167886-76-2 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)

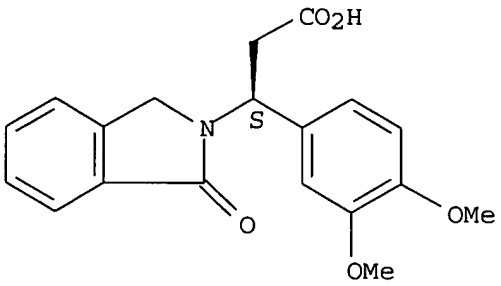


IT **167886-75-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(compns. comprising (dimethoxyphenyl)oxodihydroisoindolylpropionamide)
RN 167886-75-1 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



IT **696641-78-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(compns. comprising (dimethoxyphenyl)oxodihydroisoindolylpropionamide)
RN 696641-78-8 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo-, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L12 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:670337 HCAPLUS
DOCUMENT NUMBER: 134:157330
TITLE: Thalidomide analogue CC-3052 reduces HIV+ neutrophil apoptosis in vitro
AUTHOR(S): Guckian, M.; Dransfield, I.; Hay, P.; Dalgleish, A. G.
CORPORATE SOURCE: Division of Oncology, St George's Hospital Medical School, London, SW17 ORE, UK
SOURCE: Clinical and Experimental Immunology (2000), 121(3), 472-479
CODEN: CEXIAL; ISSN: 0009-9104
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

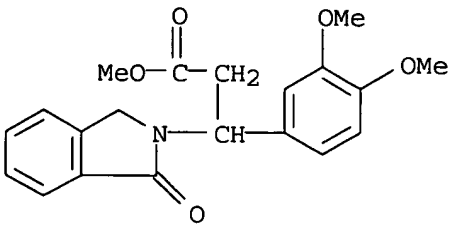
AB Recently, water-soluble analogs of thalidomide with significantly greater immunomodulatory activity and reduced side-effects than thalidomide itself have become available. The effect of thalidomide and one analog, CC-3052, on neutrophil apoptosis was examined following culture for 20 h in vitro. Apoptosis was assessed by measuring reduced CD16 expression and Annexin V binding by flow cytometry. Neither thalidomide nor CC-3052 alone had any effect on neutrophil apoptosis when used at physiol. concns. However, when used together with PGE2 (10-7M), a potent adenylate cyclase activator, CC-3052 but not thalidomide (both 10-5M) reduced apoptosis in neutrophils from normal and HIV+ donors. The reduced apoptosis could not be attributed to the ability of CC-3052 to reduce tumor necrosis

factor-α (TNF-α) production, but may have been due to its **PDE4** inhibitor properties, as it increased intracellular cAMP and mimicked the effect of dibutyryl cAMP, a membrane-permeable analog of cAMP, in increasing intracellular cAMP. The results suggest a role for thalidomide analog CC-3052 in reducing the persistent activation of the TNF-α system in HIV+ patients without markedly impairing neutrophil viability.

IT **216884-02-5**, CC 3052
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(thalidomide analog CC-3052 reduction of apoptosis by neutrophils from HIV-pos. humans)

RN 216884-02-5 HCAPLUS

CN 2H-Isoindole-2-propanoic acid, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE 'REGISTRY' ENTERED AT 14:07:10 ON 07 MAR 2006
L1 STRUCTURE UPLOADED
L2 3 S L1
L3 115 S L1 SSS FULL
L4 STRUCTURE UPLOADED
L5 4 S L4
L6 149 S L4 SSS FULL

FILE 'CAPLUS' ENTERED AT 14:10:38 ON 07 MAR 2006
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S L4

FILE 'REGISTRY' ENTERED AT 14:10:56 ON 07 MAR 2006
L8 4 S L4

FILE 'CAPLUS' ENTERED AT 14:10:57 ON 07 MAR 2006
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FILE 'HCAPLUS' ENTERED AT 14:11:15 ON 07 MAR 2006
L10 39 S L3
L11 41 S L6
L12 8 S L11 AND PDE4

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L10 ANSWER 1 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:100917 HCAPLUS
DOCUMENT NUMBER: 144:177424
TITLE: Novel isoindoline compounds and methods of their use in treating and preventing cancer
INVENTOR(S): Muller, George W.; Man, Hon-Wah
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 28 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

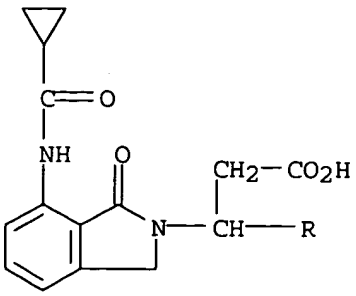
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006025457	A1	20060202	US 2004-900332	20040728
WO 2006015060	A2	20060209	WO 2005-US26679	20050727

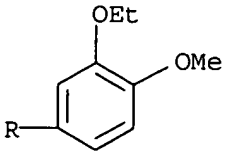
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-900332 A 20040728

AB The present invention relates to novel isoindoline compds. and pharmaceutically acceptable salts, solvates, prodrugs, and stereoisomers thereof and methods of treating and preventing cancer. Specifically, the invention relates to isoindoline compds. and methods of using the compds. in treating, preventing and/or managing cancer, diseases and disorders associated with, or characterized by, undesired angiogenesis, and diseases and disorders mediated by PDE 4, using the compds.

IT **874760-81-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(novel isoindoline compds. and methods of their use in treating and preventing cancer)
RN 874760-81-3 HCAPLUS
CN INDEX NAME NOT YET ASSIGNED





L10 ANSWER 2 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1259318 HCAPLUS
DOCUMENT NUMBER: 144:583
TITLE: Methods and compositions using selective cytokine inhibitory drugs for treatment and management of cancers and other diseases
INVENTOR(S): Zeldis, Jerome B.
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005112918	A1	20051201	WO 2004-US14002	20040505

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: WO 2004-US14002 20040505
OTHER SOURCE(S): MARPAT 144:583

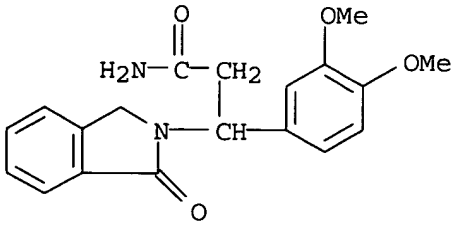
AB Methods of treating, preventing and/or managing cancer as well as and diseases and disorders associated with, or characterized by, undesired angiogenesis are disclosed. Specific methods encompass the administration of a selective cytokine inhibitory drug alone or in combination with a second active ingredient. The invention further relates to methods of reducing or avoiding adverse side effects associated with chemotherapy,

radiation therapy, hormonal therapy, biol. therapy or immunotherapy which comprise the administration of a selective cytokine inhibitory drug. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed.

IT **167886-76-2**
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytokine inhibitors for treatment and management of cancers and other diseases)

RN 167886-76-2 HCAPLUS

CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1259275 HCAPLUS
DOCUMENT NUMBER: 144:582
TITLE: Methods of using, and compositions comprising, selective cytokine inhibitory drugs for the treatment and management of myeloproliferative diseases
INVENTOR(S): Zeldis, Jerome B.
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005112917	A1	20051201	WO 2004-US14001	20040505
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: WO 2004-US14001 20040505
OTHER SOURCE(S): MARPAT 144:582

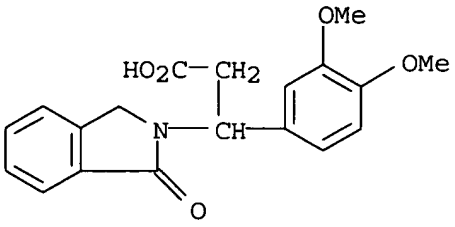
AB Methods of treating, preventing, and/or managing a myeloproliferative

disease are disclosed. Specific methods encompass the administration of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in combination with a second active agent, and/or the transplantation of blood or cells. Particular second active agent is capable of suppressing the overprodn. of hematopoietic stem cells or ameliorating one or more of the symptoms of MPD. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed.

IT **167886-75-1**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytokine inhibitors, alone or in combination with other agents, for treatment of myeloproliferative diseases)

RN 167886-75-1 HCAPLUS

CN 2H-Isoindole-2-propanoic acid, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1240579 HCAPLUS
DOCUMENT NUMBER: 143:472631
TITLE: Method of using and compositions comprising selective cytokine inhibitory drugs for the treatment and management of myelodysplastic syndromes
INVENTOR(S): Zeldis, Jerome B.
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005110085	A2	20051124	WO 2004-US11635	20040414
WO 2005110085	A3	20060209		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,

SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: WO 2004-US11635 20040414

OTHER SOURCE(S): MARPAT 143:472631

AB Methods for treating, preventing and/or managing a myelodysplastic syndrome are disclosed. Specific methods encompass the administration of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in combination with a second active ingredient, and/or blood or cells for transplantation therapy. Specific second active ingredients are capable of affecting or improving blood cell production Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed.

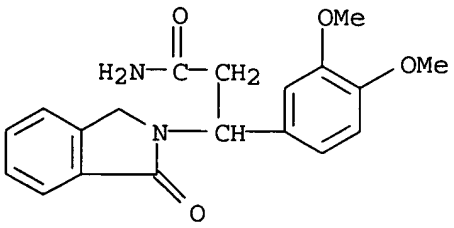
IT **167886-76-2 682359-77-9 682359-78-0**

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(cytokine inhibitors for treatment of myelodysplastic syndromes, and use with other agents)

RN 167886-76-2 HCAPLUS

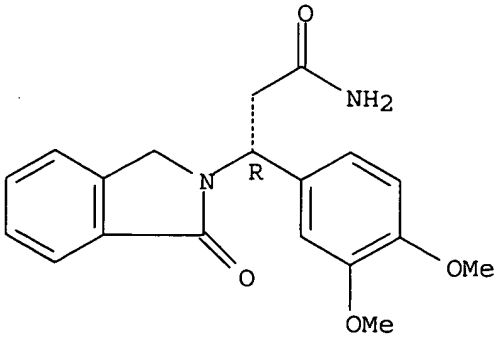
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



RN 682359-77-9 HCAPLUS

CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

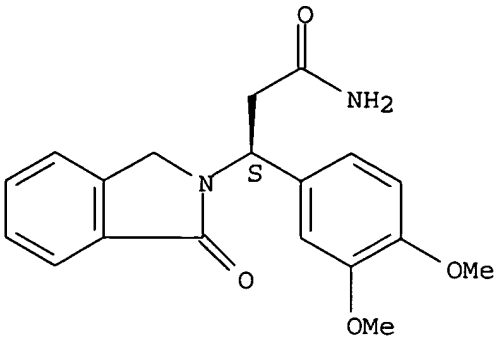
Absolute stereochemistry. Rotation (-).



RN 682359-78-0 HCAPLUS

CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo-, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L10 ANSWER 5 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1155544 HCAPLUS
DOCUMENT NUMBER: 143:416245
TITLE: Methods of using, and compositions comprising, phosphodiesterase 4 (PDE4) modulators for the treatment and management of pulmonary hypertension
INVENTOR(S): Zeldis, Jerome B.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 33 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005239867	A1	20051027	US 2005-111187	20050421
WO 2005102317	A1	20051103	WO 2005-US13597	20050421

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

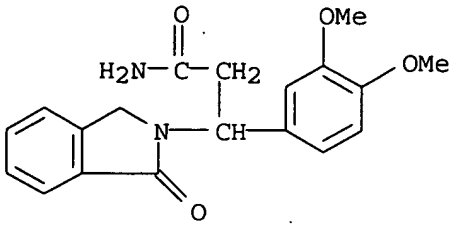
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-565174P P 20040423
OTHER SOURCE(S): MARPAT 143:416245

AB Methods of treating, preventing, and managing pulmonary hypertension are disclosed. Specific methods encompass the administration of a PDE4 modulator, or a pharmaceutically acceptable salt, solvate (e.g., hydrate), stereoisomer, clathrate, or prodrug thereof, alone or in combination with a second active agent, surgery and/or lung transplantation. Specific second active agents are capable of reducing pulmonary artery pressure. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed.

IT **167886-76-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(phosphodiesterase 4 modulators for treatment of pulmonary hypertension)
RN 167886-76-2 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



L10 ANSWER 6 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:451120 HCAPLUS
DOCUMENT NUMBER: 142:476229
TITLE: Methods of using and compositions comprising PDE4 modulators for the treatment and management of asbestos-related diseases and disorders
INVENTOR(S): Zeldis, Jerome B.
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005046592	A2	20050526	WO 2004-US37082	20041104
WO 2005046592	A3	20051215		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005142104	A1	20050630	US 2004-981190	20041103
PRIORITY APPLN. INFO.:			US 2003-518603P P	20031106
OTHER SOURCE(S):	MARPAT 142:476229			

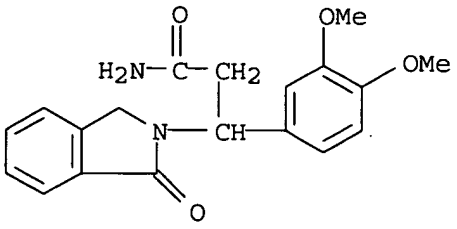
AB Methods of treating, preventing and managing an asbestos-related disease or disorder are disclosed. Specific embodiments encompass the administration of a PDE4 modulator, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in combination with a second active agent and/or chemotherapy, surgery, or radiation therapy. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in the methods of the invention are also disclosed. Treatment with 400 mg 3-(3,4-dimethoxyphenyl)-3-(1-oxo-1,3-dihydroisoindol-

2-yl)propionamide as a continuous oral daily dose is well-tolerated.

IT **167886-76-2**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as PDE4 modulator; PDE4 modulators and compns. for treatment and management of asbestos-related diseases and disorders)

RN 167886-76-2 HCAPLUS

CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



L10 ANSWER 7 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:426388 HCAPLUS

DOCUMENT NUMBER: 142:457121

TITLE: Methods of using and compositions comprising selective cytokine inhibitory drug for treatment, modification and management of pain

INVENTOR(S): Zeldis, Jerome B.; Faleck, Herbert; Manning, Donald C.

PATENT ASSIGNEE(S): Celgene Corporation, USA

SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005043971	A2	20050519	WO 2004-US12722	20040423
WO 2005043971	A3	20050714		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005203142	A1	20050915	US 2003-693794	20031023
PRIORITY APPLN. INFO.:			US 2003-693794 A	20031023
			US 2002-421003P P	20021024

OTHER SOURCE(S): MARPAT 142:457121

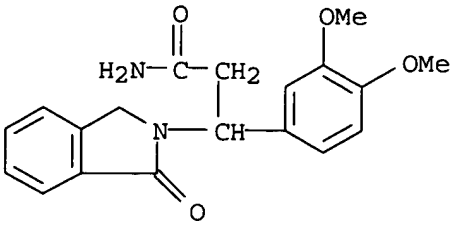
AB Methods of treating, preventing, modifying and managing various types of pain are disclosed. Specific methods comprise the administration of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt,

solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in combination with a second active agent and/or surgery, psychol. or phys. therapy. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed.

IT **167886-76-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytokine inhibitors, alone or in combination with other agents, for treatment of pain)

RN 167886-76-2 HCAPLUS

CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



L10 ANSWER 8 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:780510 HCAPLUS
DOCUMENT NUMBER: 141:277486
TITLE: A preparation of 7-aminoisoindolone derivatives
INVENTOR(S): Man, Hon-Wah; Muller, George W.; Zhang, Weihong
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 109 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004080423	A2	20040923	WO 2004-US7743	20040312
WO 2004080423	A3	20041104		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2518584	AA	20040923	CA 2004-2518584	20040312
US 2004254214	A1	20041216	US 2004-798317	20040312
EP 1605896	A2	20051221	EP 2004-720448	20040312
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				

PRIORITY APPLN. INFO.: US 2003-454155P P 20030312

WO 2004-US7743 W 20040312

OTHER SOURCE(S): MARPAT 141:277486
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

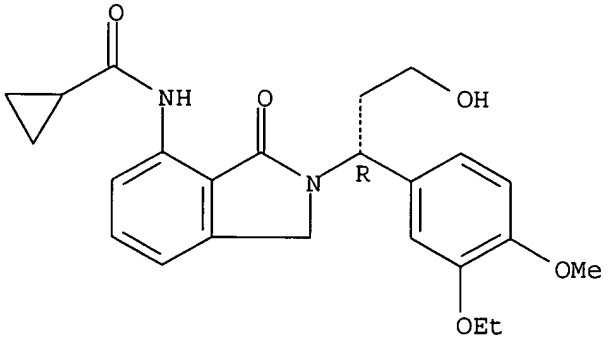
AB The invention relates to a preparation of 7-aminoisoindole derivs. of formula I [wherein: Y is C(O), CH2, CH2C(O), or SO2; X is H; Z is -alkyl-CO2H, alkyl, -alkyl-OH, or -alkyl-NH2, etc.; R1 and R2 are independently selected from (cyclo)alkyl or -alkyl-cycloalkyl], useful for treatment, prevention or management of cancer, inflammatory bowel disease, and myelodysplastic syndrome, etc. (no biol. data). For instance, isoindole derivative II was prepared via heterocyclization of aminopropanol derivative III and benzoic acid derivative IV with a yield of 64% (example 1).

IT **760958-78-9P 760958-80-3P 760958-88-1P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of aminoisoindolone derivs. via heterocyclization of aminopropanol derivs. and benzoic acid derivs.)

RN 760958-78-9 HCAPLUS

CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-hydroxypropyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

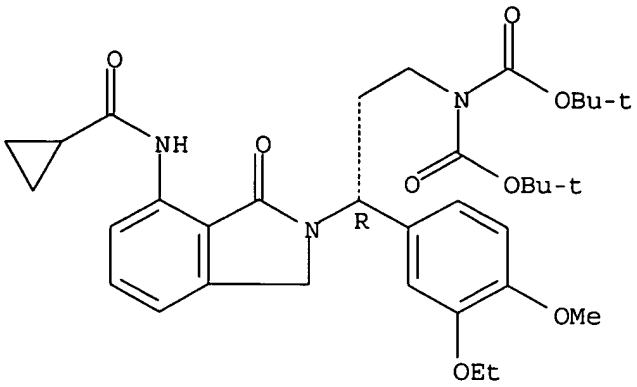
Absolute stereochemistry.



RN 760958-80-3 HCAPLUS

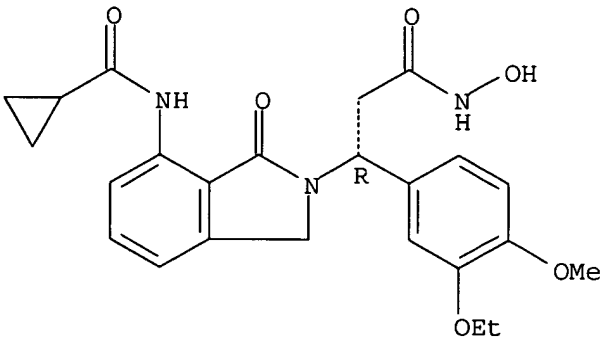
CN Imidodicarbonic acid, [(3R)-3-[7-[(cyclopropylcarbonyl)amino]-1,3-dihydro-1-oxo-2H-isoindol-2-yl]-3-(3-ethoxy-4-methoxyphenyl)propyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



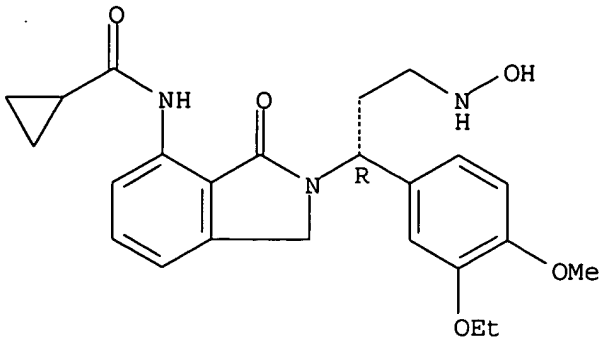
RN 760958-88-1 HCAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N-hydroxy-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



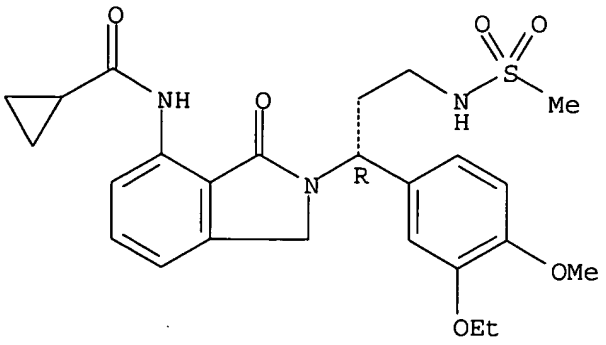
IT **760958-82-5P 760958-83-6P 760958-85-8P**
760958-86-9P 760958-87-0P 760958-90-5P
760958-91-6P 760958-93-8P 760958-96-1P
760958-97-2P 760958-98-3P 760958-99-4P
760959-04-4P 760959-06-6P 760959-09-9P
760959-12-4P 760959-13-5P 760959-14-6P
760959-15-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminoisoindolone derivs. via heterocyclization of aminopropanol derivs. and benzoic acid derivs.)
RN 760958-82-5 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-(hydroxyamino)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



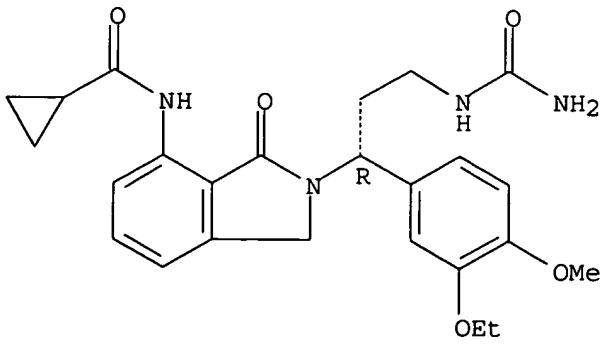
RN 760958-83-6 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-[(methylsulfonyl)amino]propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 760958-85-8 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-3-[(aminocarbonyl)amino]-1-(3-ethoxy-4-methoxyphenyl)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

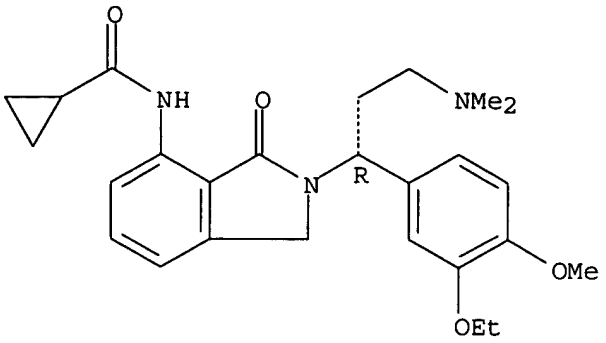
Absolute stereochemistry.



RN 760958-86-9 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-3-(dimethylamino)-1-(3-ethoxy-4-

methoxyphenyl)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]-, monohydrochloride (9CI) (CA INDEX NAME)

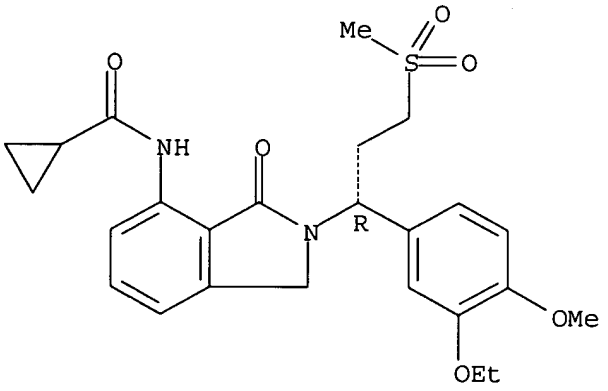
Absolute stereochemistry.



● HCl

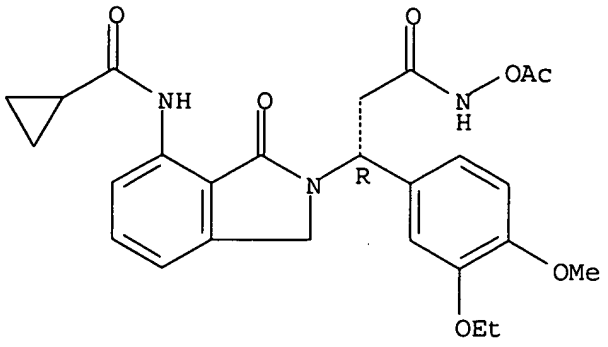
RN 760958-87-0 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-(methylsulfonyl)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



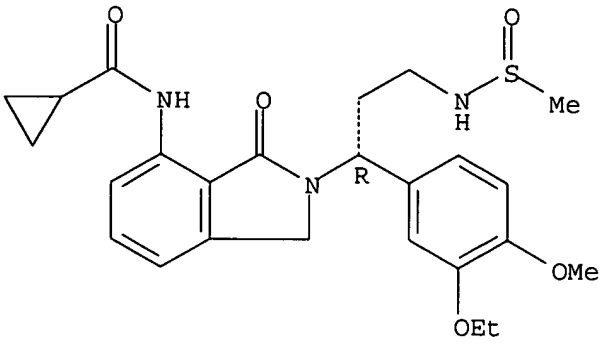
RN 760958-90-5 HCAPLUS
CN 2H-Isoindole-2-propanamide, N-(acetyloxy)-7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



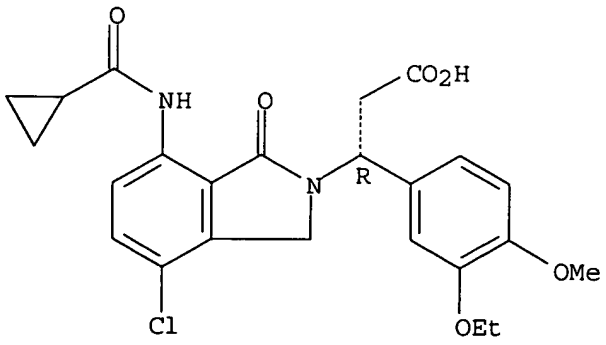
RN 760958-91-6 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-[(methylsulfinyl)amino]propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 760958-93-8 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, 4-chloro-7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

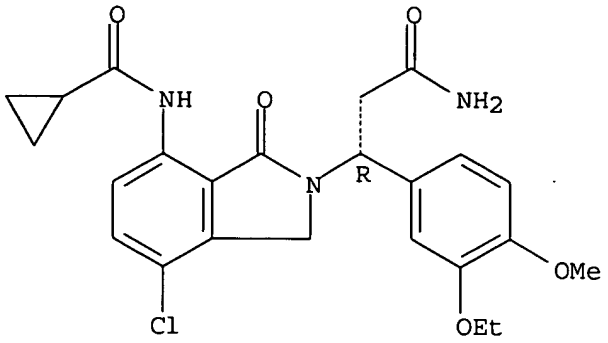
Absolute stereochemistry.



RN 760958-96-1 HCAPLUS
CN 2H-Isoindole-2-propanamide, 4-chloro-7-[(cyclopropylcarbonyl)amino]-β-

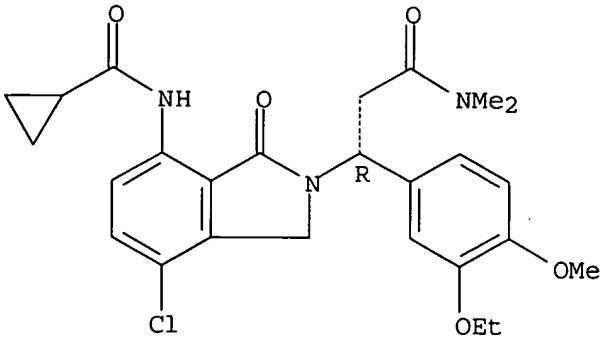
(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



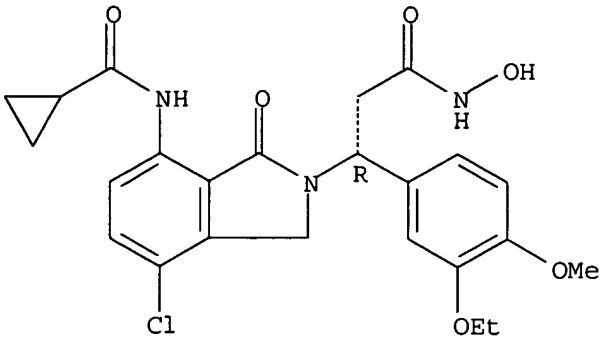
RN 760958-97-2 HCAPLUS
CN 2H-Isoindole-2-propanamide, 4-chloro-7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



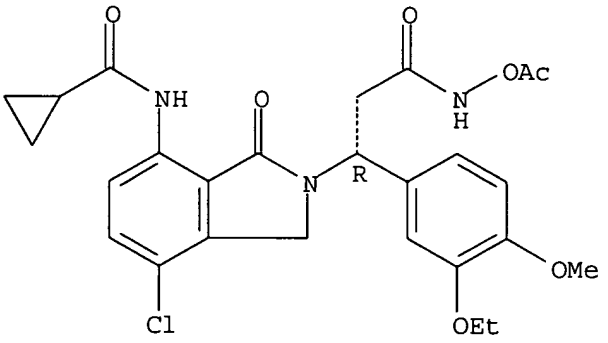
RN 760958-98-3 HCAPLUS
CN 2H-Isoindole-2-propanamide, 4-chloro-7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N-hydroxy-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

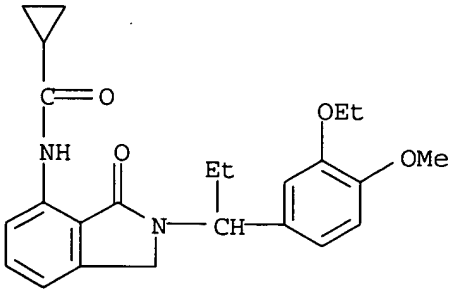


RN 760958-99-4 HCAPLUS
CN 2H-Isoindole-2-propanamide, N-(acetyloxy)-4-chloro-7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

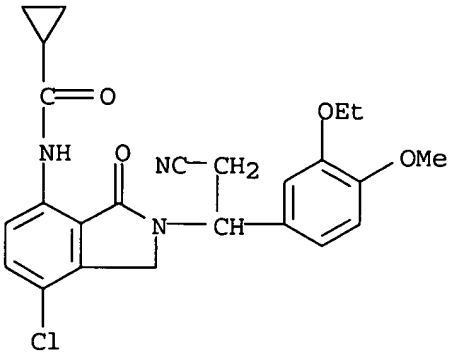
Absolute stereochemistry.



RN 760959-04-4 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

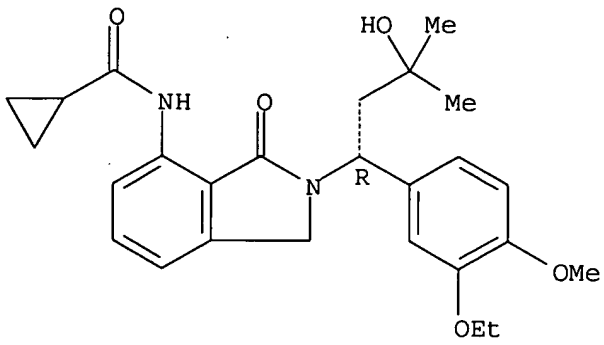


RN 760959-06-6 HCAPLUS
CN Cyclopropanecarboxamide, N-[7-chloro-2-[2-cyano-1-(3-ethoxy-4-methoxyphenyl)ethyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)



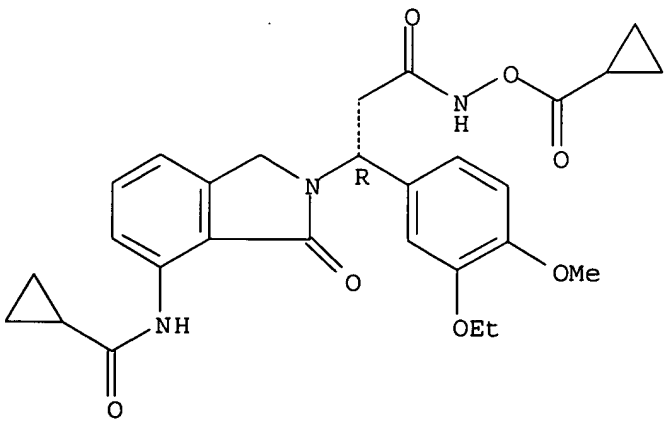
RN 760959-09-9 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-hydroxy-3-methylbutyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 760959-12-4 HCAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-N-[(cyclopropylcarbonyl)oxy]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

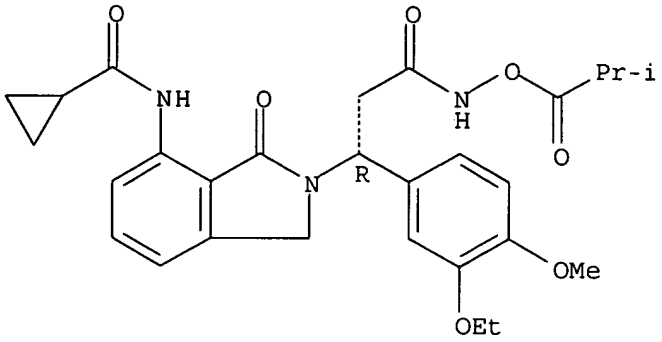
Absolute stereochemistry.



RN 760959-13-5 HCAPLUS

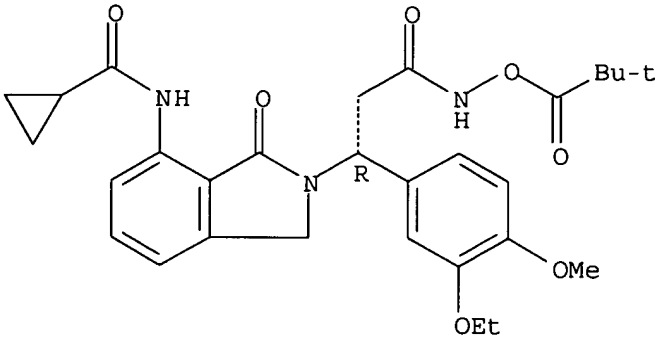
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N-(2-methyl-1-oxopropoxy)-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



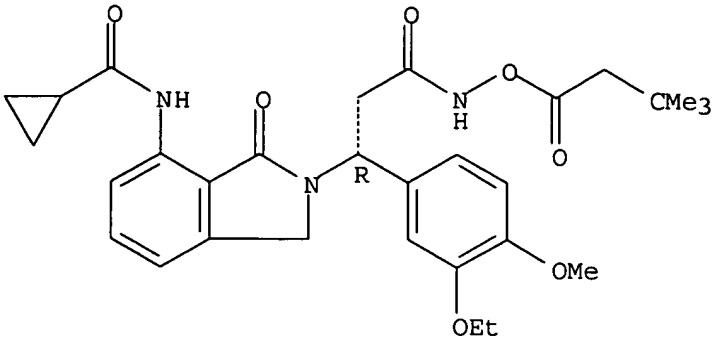
RN 760959-14-6 HCAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-N-(2,2-dimethyl-1-oxopropoxy)-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



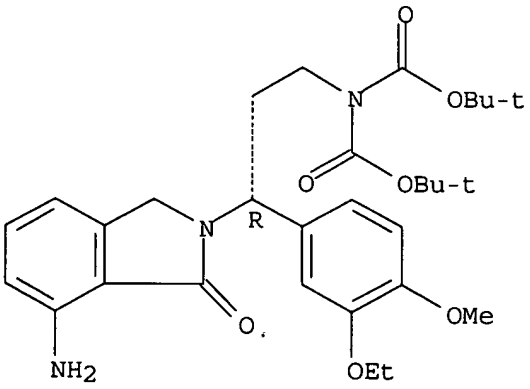
RN 760959-15-7 HCAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-N-(3,3-dimethyl-1-oxobutoxy)-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



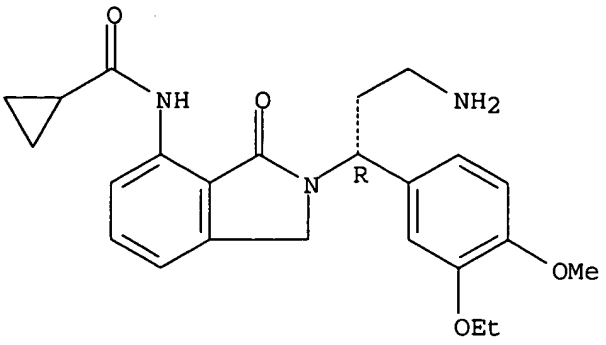
IT **760958-81-4 760958-84-7 760958-89-2**
760958-94-9 760959-05-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of aminoisoindolone derivs. via heterocyclization of aminopropanol derivs. and benzoic acid derivs.)
RN 760958-81-4 HCAPLUS
CN Imidodicarbonic acid, [(3R)-3-(7-amino-1,3-dihydro-1-oxo-2H-isoindol-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propyl]-, bis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



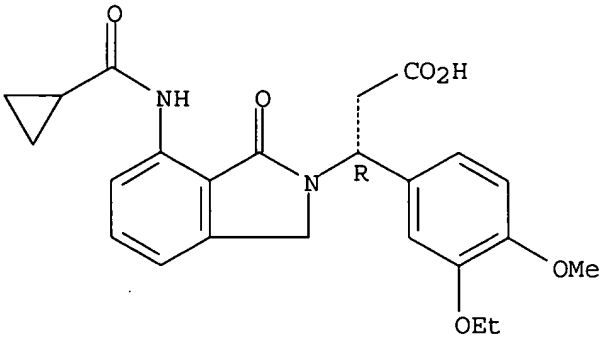
RN 760958-84-7 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-3-amino-1-(3-ethoxy-4-methoxyphenyl)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



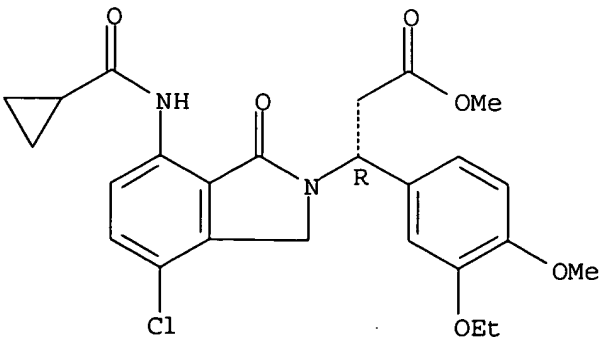
RN 760958-89-2 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, 7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



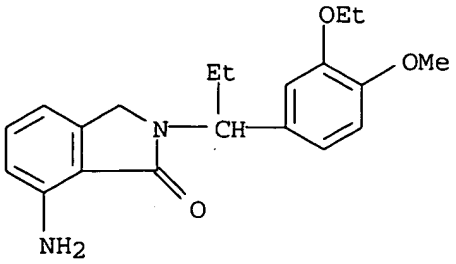
RN 760958-94-9 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, 4-chloro-7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, methyl ester, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



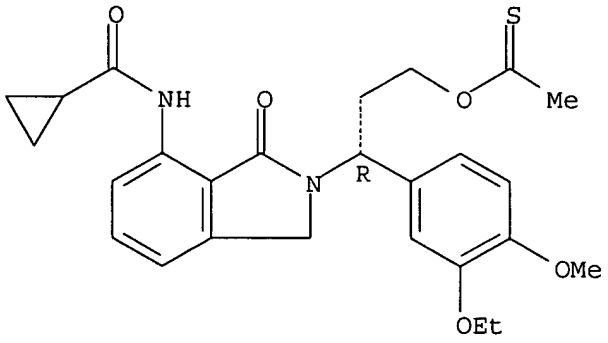
RN 760959-05-5 HCAPLUS
CN 1H-Isoindol-1-one, 7-amino-2-[1-(3-ethoxy-4-methoxyphenyl)propyl]-2,3-

dihydro- (9CI) (CA INDEX NAME)



IT **760958-92-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aminoisoindolone derivs. via heterocyclization of aminopropanol derivs. and benzoic acid derivs.)
RN 760958-92-7 HCAPLUS
CN Ethanethioic acid, O-[(3R)-3-[7-[(cyclopropylcarbonyl)amino]-1,3-dihydro-1-oxo-2H-isoindol-2-yl]-3-(3-ethoxy-4-methoxyphenyl)propyl] ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 9 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:780509 HCAPLUS
DOCUMENT NUMBER: 141:295861
TITLE: A preparation of novel isoindolone derivatives, useful as PDE4 inhibitors
INVENTOR(S): Man, Hon-Wah; Muller, George W.
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004080422	A2	20040923	WO 2004-US7742	20040312
WO 2004080422	A3	20041028		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2518513	AA	20040923	CA 2004-2518513	20040312
US 2004259873	A1	20041223	US 2004-798372	20040312
US 6911464	B2	20050628		
EP 1606256	A2	20051221	EP 2004-720480	20040312
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
US 2005203090	A1	20050915	US 2005-124280	20050509
PRIORITY APPLN. INFO.:			US 2003-454149P	P 20030312
			US 2004-798372	A3 20040312
			WO 2004-US7742	W 20040312

OTHER SOURCE(S): MARPAT 141:295861
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

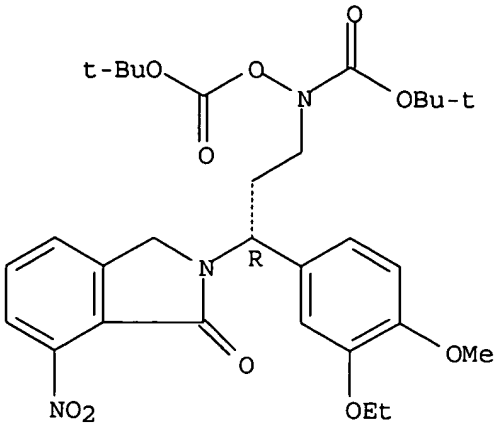
AB The invention relates to a preparation of novel isoindolone derivs. of formula I [wherein: Y is C(O), CH2, CH2C(O), or SO2; R1 and R2 are independently selected from (cyclo)alkyl, CF2H, CF3, or CH2CHF2, etc.; Z1 is H, alkyl, NH2, or NH2, etc.; Z2 is H or CHO, -C(O)-alkyl, or -C(O)Ph, etc.; X1, X2, X3, and X4 are independently selected from H, halogen, NO2, CF3, alkyl, or alkylimidazolyl, etc.; R3 and R4 are independently H or alkyl], useful for treatment or prevention of various diseases and disorders, for example, diseases associated with PDE4 (no biol. data). For instance, isoindolone derivative II was prepared via amination of N-(hydroxypropyl)isoindolone derivative III by N,O-(tert-butoxycarbonyl)hydroxylamine with a yield of 78%.

IT **761434-15-5P 761434-16-6P 761434-20-2P 761434-23-5P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of novel isoindolone derivs. useful as PDE4 inhibitors)

RN 761434-15-5 HCAPLUS

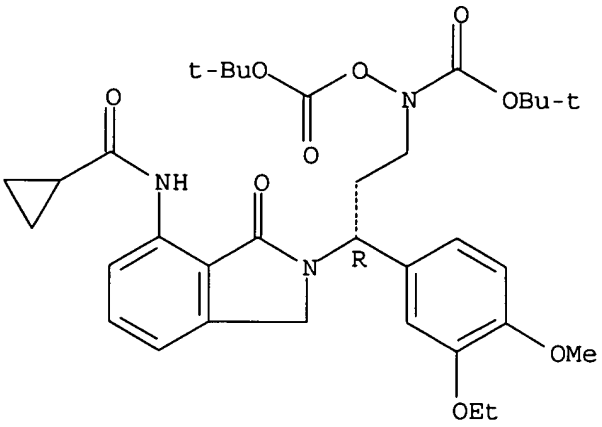
CN Carbamic acid, [(3R)-3-(1,3-dihydro-7-nitro-1-oxo-2H-isoindol-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propyl][[(1,1-dimethylethoxy)carbonyl]oxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



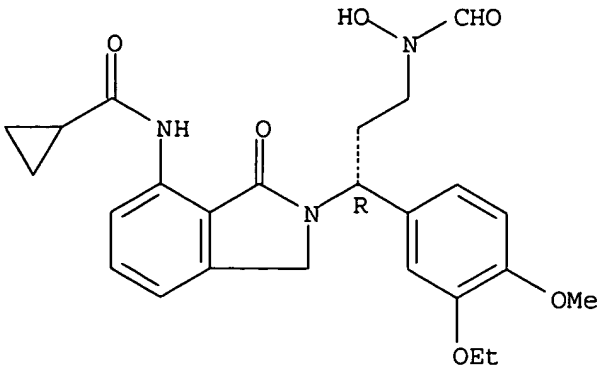
RN 761434-16-6 HCAPLUS
CN Carbamic acid, [(3R)-3-[7-[(cyclopropylcarbonyl)amino]-1,3-dihydro-1-oxo-2H-isoindol-2-yl]-3-(3-ethoxy-4-methoxyphenyl)propyl][[(1,1-dimethylethoxy)carbonyl]oxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



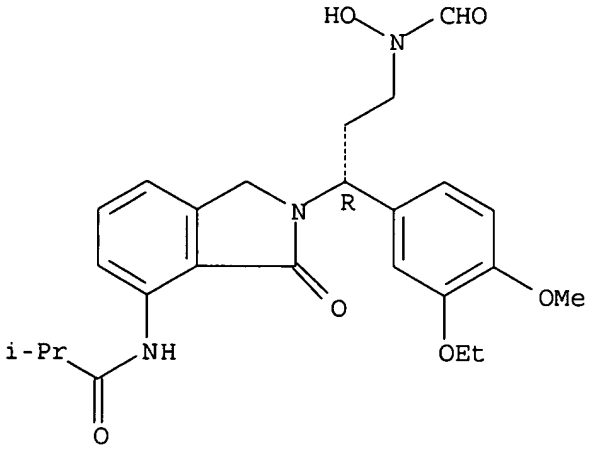
RN 761434-20-2 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-(formylhydroxyamino)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

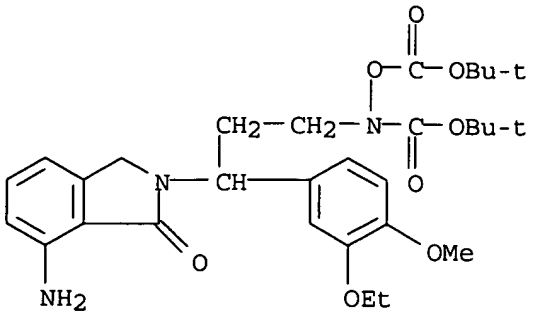


RN 761434-23-5 HCAPLUS
CN Propanamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-(formylhydroxyamino)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

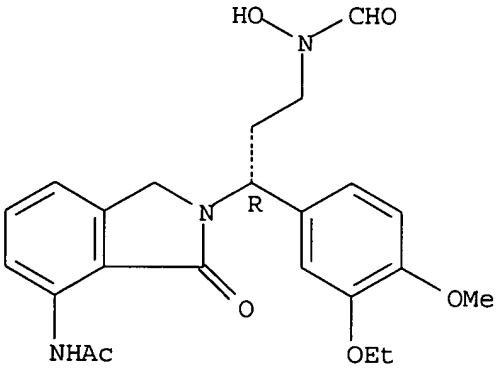


IT **761434-18-8P 761434-21-3P 761434-27-9P 761434-28-0P 761434-29-1P 761434-30-4P 761434-32-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel isoindolone derivs. useful as PDE4 inhibitors)
RN 761434-18-8 HCAPLUS
CN Carbamic acid, [3-(7-amino-1,3-dihydro-1-oxo-2H-isoindol-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propyl][[(1,1-dimethylethoxy)carbonyl]oxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



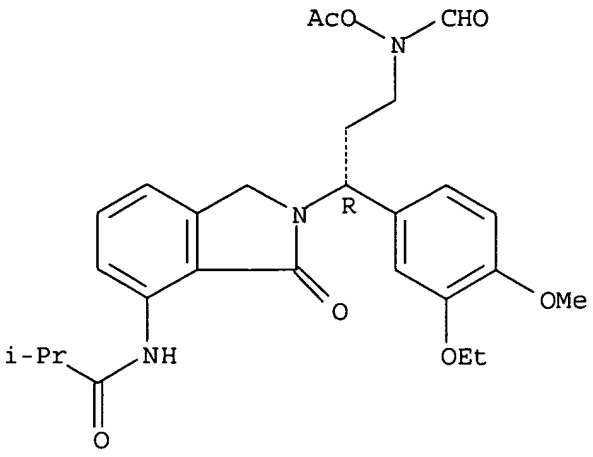
RN 761434-21-3 HCAPLUS
CN Acetamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-(formylhydroxyamino)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



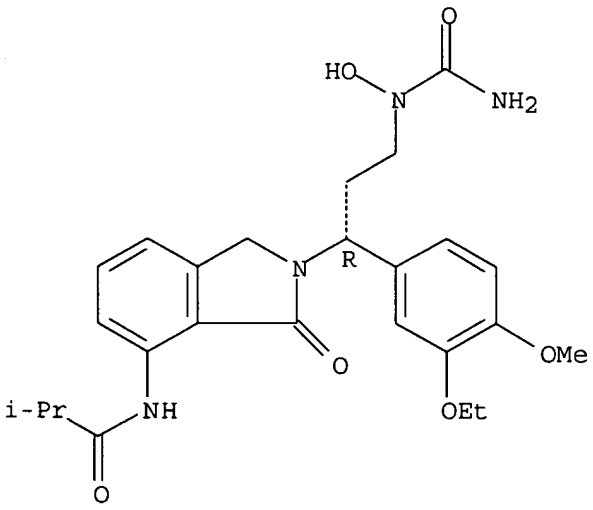
RN 761434-27-9 HCAPLUS
CN Propanamide, N-[2-[(1R)-3-[(acetyloxy)formylamino]-1-(3-ethoxy-4-methoxyphenyl)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



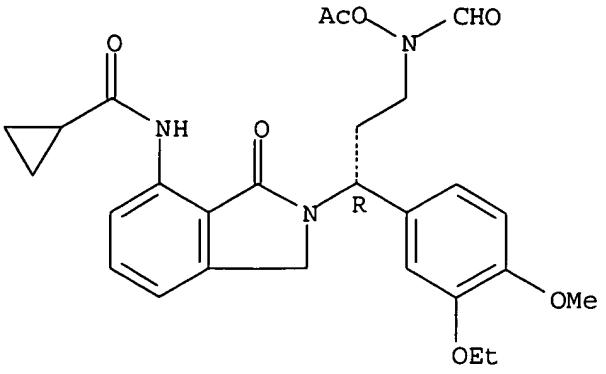
RN 761434-28-0 HCAPLUS
CN Propanamide, N-[2-[(1R)-3-[(aminocarbonyl)hydroxyamino]-1-(3-ethoxy-4-methoxyphenyl)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

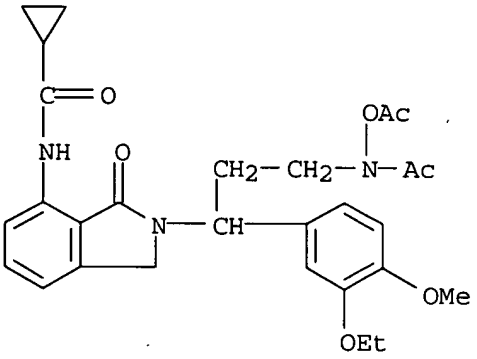


RN 761434-29-1 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-3-[(acetyloxy)formylamino]-1-(3-ethoxy-4-methoxyphenyl)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

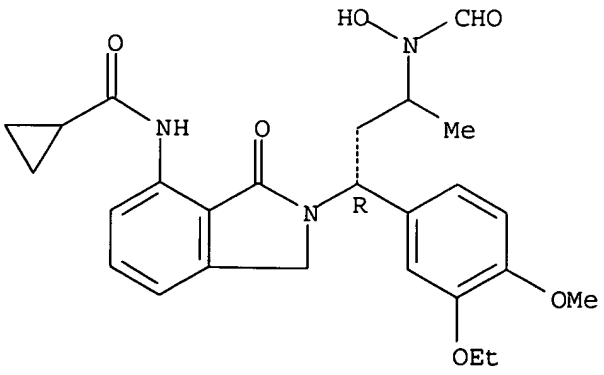


RN 761434-30-4 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[3-[acetyl(acetyloxy)amino]-1-(3-ethoxy-4-methoxyphenyl)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)



RN 761434-32-6 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-(formylhydroxyamino)butyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

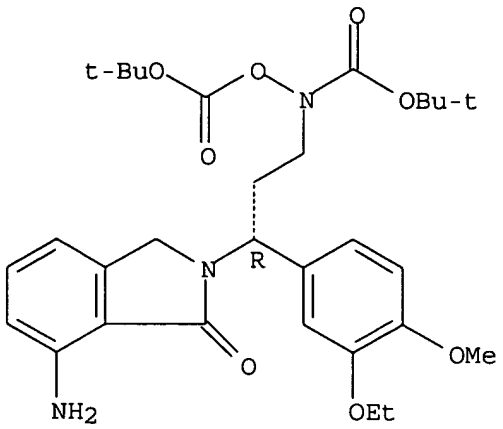


IT **761434-17-7 761434-19-9 761434-22-4**

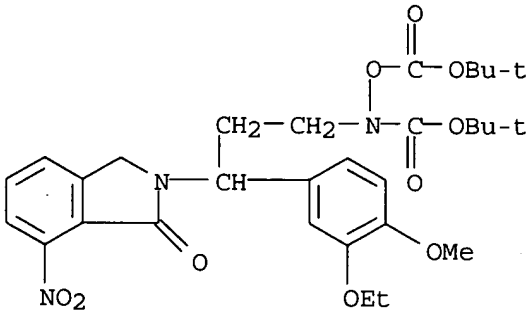
761434-24-6 761434-31-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of novel isoindolone derivs. useful as PDE4 inhibitors)

RN 761434-17-7 HCAPLUS
CN Carbamic acid, [(3R)-3-(7-amino-1,3-dihydro-1-oxo-2H-isoindol-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propyl][[(1,1-dimethylethoxy)carbonyl]oxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

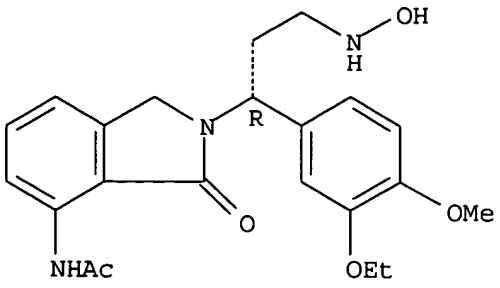


RN 761434-19-9 HCAPLUS
CN Carbamic acid, [3-(1,3-dihydro-7-nitro-1-oxo-2H-isoindol-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propyl][[(1,1-dimethylethoxy)carbonyl]oxy]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



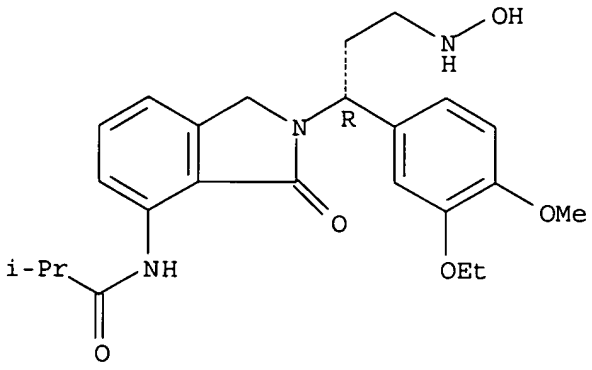
RN 761434-22-4 HCAPLUS
CN Acetamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-(hydroxyamino)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

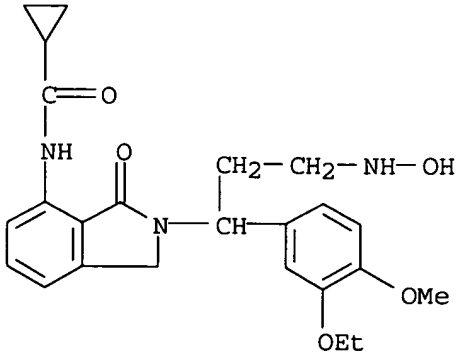


RN 761434-24-6 HCAPLUS
CN Propanamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-(hydroxyamino)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



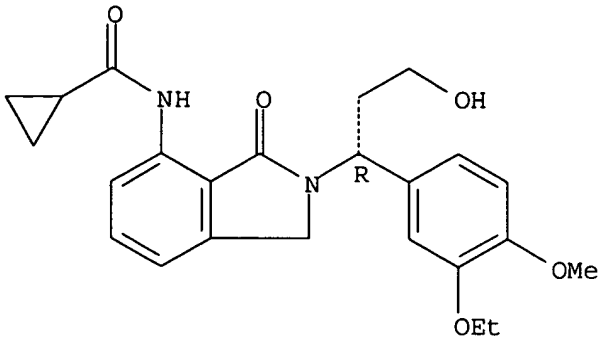
RN 761434-31-5 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[1-(3-ethoxy-4-methoxyphenyl)-3-(hydroxyamino)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)



IT **760958-78-9P 760958-82-5P 761434-14-4P 761434-34-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

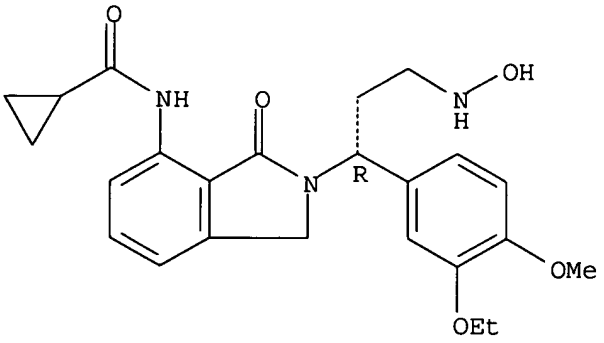
(preparation of novel isoindolone derivs. useful as PDE4 inhibitors)
RN 760958-78-9 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-hydroxypropyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



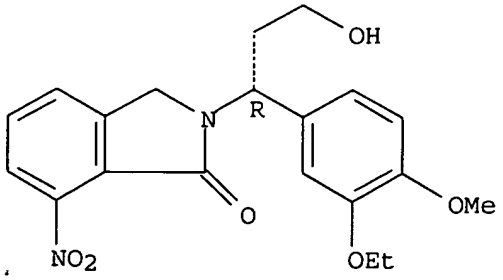
RN 760958-82-5 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-(hydroxyamino)propyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



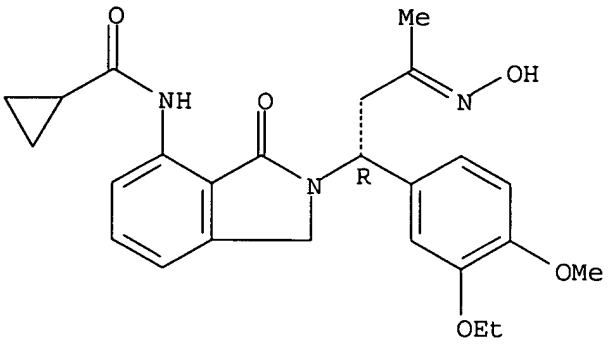
RN 761434-14-4 HCAPLUS
CN 1H-Isoindol-1-one, 2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-hydroxypropyl]-2,3-dihydro-7-nitro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 761434-34-8 HCAPLUS
CN Cyclopropanecarboxamide, N-[2-[(1R)-1-(3-ethoxy-4-methoxyphenyl)-3-(hydroxyimino)butyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



L10 ANSWER 10 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:739745 HCAPLUS
DOCUMENT NUMBER: 141:248733
TITLE: Methods of using and compositions comprising selective cytokine inhibitory drugs for the treatment and management of disorders of the central nervous system
INVENTOR(S): Schafer, Peter H.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 28 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004175382	A1	20040909	US 2004-794877	20040305
CA 2517845	AA	20040923	CA 2004-2517845	20040305
WO 2004080393	A2	20040923	WO 2004-US6782	20040305
WO 2004080393	A3	20041202		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1605935	A2	20051221	EP 2004-717992	20040305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				

PRIORITY APPLN. INFO.: US 2003-452374P P 20030306
WO 2004-US6782 W 20040305

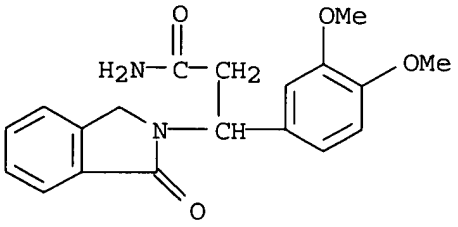
OTHER SOURCE(S): MARPAT 141:248733

AB Methods of treating, preventing and/or managing central nervous system disorders, such as Parkinson disease, Alzheimer disease, mild cognitive impairment, Huntington disease, Amytophic Lateral Sclerosis, depression and defective long-term memory, and related syndromes are disclosed. Specific methods encompass the administration of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in combination with a second active ingredient. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed. The effect of 3-(3,4-dimethoxy-phenyl)-3-(1-oxo-1,3-dihydro-isoindol-2-yl)-propionamide on TNF-α production in LPS-induced human peripheral blood mononuclear cells (PBMC) was examined

IT **167886-76-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods of using and compns. comprising selective cytokine inhibitory drugs for treatment and management of disorders of central nervous system)

RN 167886-76-2 HCAPLUS

CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



L10 ANSWER 11 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:589381 HCAPLUS
DOCUMENT NUMBER: 141:140314
TITLE: Preparation of 2-(fluoroalkoxyphenylalkyl)-1,3-dihydroisoindolones as PDE4, TNF-α, and/or MMP inhibitors
INVENTOR(S): Muller, George W.; Man, Hon-Wah; Zhang, Weihong
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004060313	A2	20040722	WO 2003-US41568	20031229
WO 2004060313	A3	20050915		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,

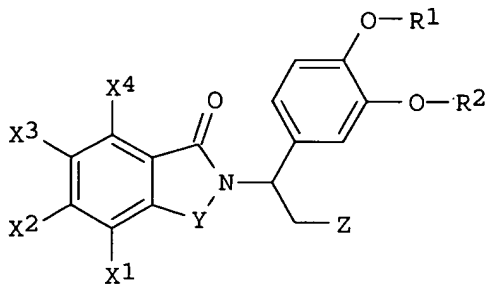
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2511843	AA	20040722	CA 2003-2511843	20031229
US 2004204448	A1	20041014	US 2003-748085	20031229
EP 1587474	A2	20051026	EP 2003-808605	20031229
EP 1587474	A3	20051102		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

PRIORITY APPLN. INFO.:	US 2002-436975P	P	20021230
	WO 2003-US41568	W	20031229

OTHER SOURCE(S): MARPAT 141:140314
GI



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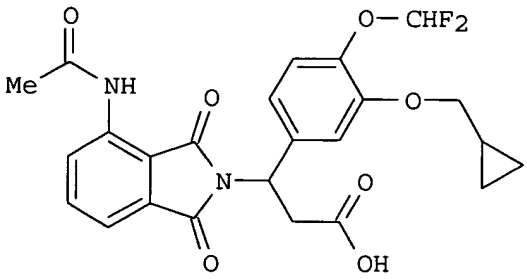


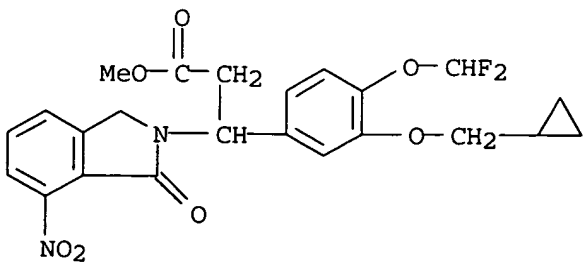
II

AB Title compds. I [wherein X1-X4 = independently H, halo, NO2, NH2, CF3, alkyl, cycloalkyl(alkyl), NR7R8-(alkyl), R8CONH-(alkyl), NR7R8CONH-(alkyl), R8OCONH-(alkyl), R8O-(alkyl), imidazolyl(alkyl), pyrrolyl(alkyl), oxadiazolyl(alkyl), triazolyl(alkyl); or X1 and X2 or X2 and X3 or X3 and X4 may be taken together to form a (hetero)cycloalkyl ring; Y = CO, CH2, CH2CO, COCH2, SO2; Z = H, COR3, alkylsulfonyl(alkyl), alkyl, CH2OH, alkoxymethyl, CN; R1 and R2 = independently CHF2, alkyl, cycloalkyl(alkyl); at least one of R1 and R2 = CHF2; R3 = NR4R5, alkyl, OH, alkoxy, (un)substituted Ph, PhCH2; R4 and R5 = independently H, alkyl, OH, OCOR6; R6 = alkyl(amino), Ph, PhCH2, aryl; R7 and R8 = independently H, alkyl, cycloalkyl(alkyl), NR7R8-alkyl, R8O-alkyl, Ph, PhCH2, aryl; or pharmaceutically acceptable salts, hydrates, solvates, clathrates, stereoisomers, and prodrugs thereof] were prepared For example, alkylation of 3,4-dihydroxybenzaldehyde with chlorodifluoromethane in the presence of

K2CO3 in DMF gave 4-difluoromethoxy-3-hydroxybenzaldehyde (15%), which was further alkylated with bromomethylcyclopropane under the same conditions to afford 3-cyclopropylmethoxy-4-difluoromethoxybenzaldehyde (100%). Reaction of the benzaldehyde with ammonium acetate in 95% EtOH, followed by addition of malonic acid provided 3-amino-3-(3-cyclopropylmethoxy-4-difluoromethoxyphenyl)propionic acid (52%). Condensation of the amine with 3-acetamidophthalic anhydride using sodium acetate in AcOH yielded the isoindoledione II (85%). I and their pharmaceutical compns., optionally in combination with another therapeutic agent, are useful for the treatment or prevention of diseases associated with phosphodiesterase 4 (PDE4) inhibition, abnormal tumor necrosis factor α (TNF-α) levels , and/or matrix metalloproteinase (MMP) inhibition, such as myelodysplastic syndrome, myeloproliferative disease, complex regional pain syndrome, cancer, inflammatory diseases, and autoimmune diseases (no data).

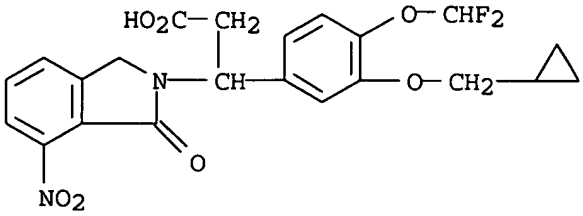
IT **725256-76-8P**, 3-[3-(Cyclopropylmethoxy)-4-difluoromethoxyphenyl]-3-(7-nitro-1-oxo-1,3-dihydroisoindol-2-yl)propionic acid methyl ester **725256-77-9P**, 3-[3-(Cyclopropylmethoxy)-4-difluoromethoxyphenyl]-3-(7-nitro-1-oxo-1,3-dihydroisoindol-2-yl)propionic acid **725256-78-0P**, 3-[3-(Cyclopropylmethoxy)-4-difluoromethoxyphenyl]-3-(7-nitro-1-oxo-1,3-dihydroisoindol-2-yl)-N,N-dimethylpropionamide **725256-83-7P**, 3-[7-(Cyclopropylcarbonylamino)-1-oxo-1,3-dihydroisoindol-2-yl]-3-(4-difluoromethoxy-3-ethoxyphenyl)propionic acid methyl ester **725256-84-8P**, 3-(7-Amino-1-oxo-1,3-dihydroisoindol-2-yl)-3-(4-difluoromethoxy-3-ethoxyphenyl)propionic acid methyl ester **725256-85-9P**, 3-(7-Acetylamino-1-oxo-1,3-dihydroisoindol-2-yl)-3-(4-difluoromethoxy-3-ethoxyphenyl)propionic acid methyl ester **725256-86-0P**, 3-[7-(Acetylamino)-1-oxo-1,3-dihydroisoindol-2-yl]-3-(4-difluoromethoxy-3-ethoxyphenyl)propionic acid **725256-87-1P**, 3-[7-(Cyclopropylcarbonylamino)-1-oxo-1,3-dihydroisoindol-2-yl]-3-(4-difluoromethoxy-3-ethoxyphenyl)propionic acid **725257-12-5P**, 3-[3,4-Bis(difluoromethoxy)phenyl]-3-[7-(cyclopropylcarbonylamino)-1-oxo-1,3-dihydroisoindol-2-yl]propionic acid
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(PDE4, TNF-α, and/or MMP inhibitor; preparation of (fluoroalkoxyphenylalkyl)isoindolones as PDE4, TNF-α, and/or MMP inhibitors for treatment of inflammatory diseases, autoimmune diseases, cancer, and pain)

RN 725256-76-8 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-[3-(cyclopropylmethoxy)-4-(difluoromethoxy)phenyl]-1,3-dihydro-7-nitro-1-oxo-, methyl ester (9CI) (CA INDEX NAME)

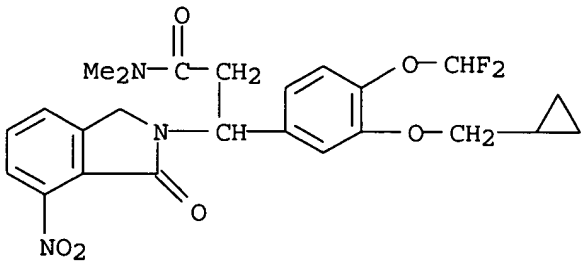


RN 725256-77-9 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-[3-(cyclopropylmethoxy)-4-

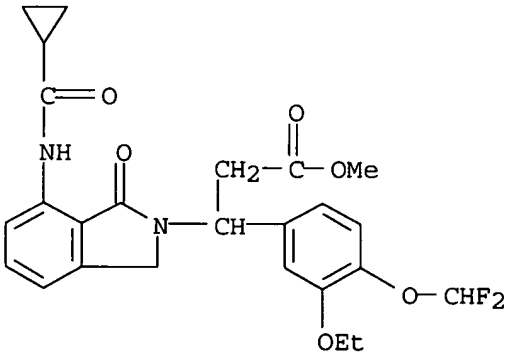
(difluoromethoxy)phenyl]-1,3-dihydro-7-nitro-1-oxo- (9CI) (CA INDEX NAME)



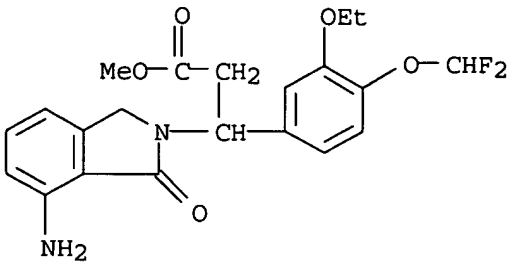
RN 725256-78-0 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-[3-(cyclopropylmethoxy)-4-(difluoromethoxy)phenyl]-1,3-dihydro-N,N-dimethyl-7-nitro-1-oxo- (9CI) (CA INDEX NAME)



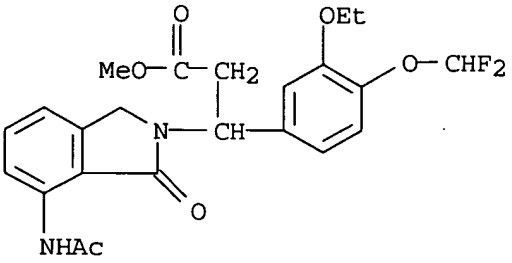
RN 725256-83-7 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, 7-[(cyclopropylcarbonyl)amino]-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



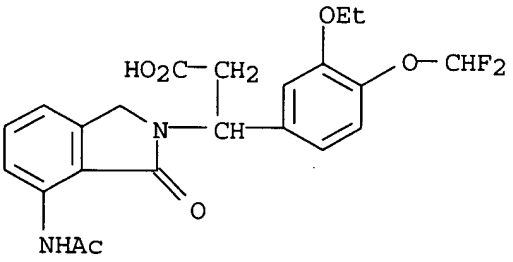
RN 725256-84-8 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, 7-amino-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



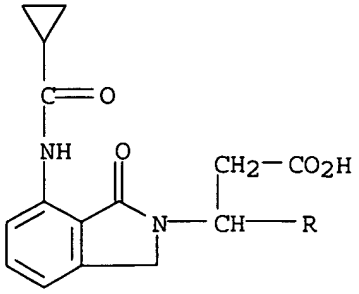
RN 725256-85-9 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, 7-(acetylamino)-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-1-oxo-, methyl ester (9CI) (CA INDEX NAME)

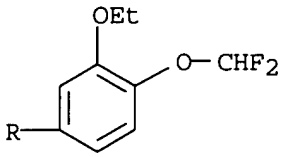


RN 725256-86-0 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, 7-(acetylamino)-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)

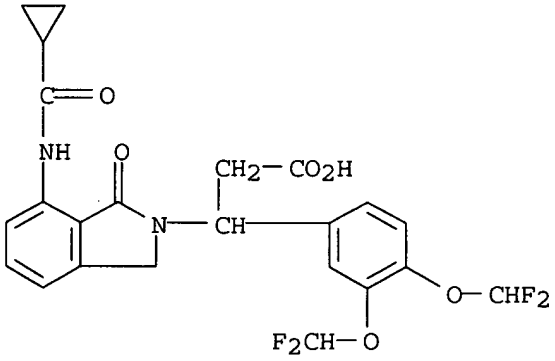


RN 725256-87-1 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, 7-[(cyclopropylcarbonyl)amino]-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)





RN 725257-12-5 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-[3,4-bis(difluoromethoxy)phenyl]-7-[(cyclopropylcarbonyl)amino]-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



IT **725256-79-1P**, 3-(7-Amino-1-oxo-1,3-dihydroisoindol-2-yl)-3-[3-(cyclopropylmethoxy)-4-difluoromethoxyphenyl]-N,N-dimethylpropionamide **725256-82-6P**, 3-(4-Difluoromethoxy-3-ethoxyphenyl)-3-(7-nitro-1-oxo-1,3-dihydroisoindol-2-yl)propionic acid methyl ester **725256-88-2P**, Cyclopropanecarboxylic acid N-[2-[2-carbamoyl-1-(4-difluoromethoxy-3-ethoxyphenyl)ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl]amide **725256-89-3P**, Cyclopropanecarboxylic acid N-[2-[1-(4-difluoromethoxy-3-ethoxyphenyl)-2-(dimethylcarbamoyl)ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl]amide **725256-90-6P**, Cyclopropanecarboxylic acid N-[2-[1-(4-difluoromethoxy-3-ethoxyphenyl)-2-hydroxycarbamoylethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl]amide **725256-91-7P**, 3-(7-Acetylamino-1-oxo-1,3-dihydroisoindol-2-yl)-3-(4-difluoromethoxy-3-ethoxyphenyl)propionamide **725256-92-8P**, 3-(7-Acetylamino-1-oxo-1,3-dihydroisoindol-2-yl)-3-(4-difluoromethoxy-3-ethoxyphenyl)-N,N-dimethylpropionamide **725256-93-9P**, 3-(7-Acetylamino-1-oxo-1,3-dihydroisoindol-2-yl)-3-(4-difluoromethoxy-3-ethoxyphenyl)-N-hydroxypropionamide **725257-02-3P**, Cyclopropanecarboxylic acid N-[2-[2-carbamoyl-1-(4-difluoromethoxy-3-

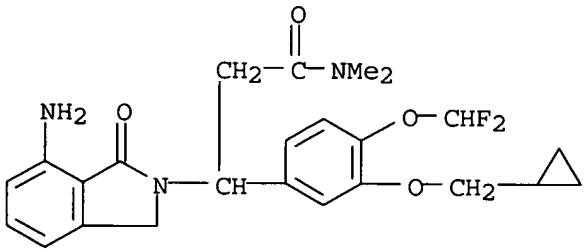
ethoxyphenyl)ethyl]-7-chloro-3-oxo-2,3-dihydro-1H-isoindol-4-yl]amide **725257-05-6P**, N-[2-[1-(4-Difluoromethoxy-3-ethoxyphenyl)-3-(morpholin-4-yl)-3-oxopropyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl]acetamide **725257-08-9P**, 3-[3,4-Bis(difluoromethoxy)phenyl]-3-[4-chloro-7-(cyclopropylcarbonylamino)-1-oxo-1,3-dihydroisoindol-2-yl]propionic acid methyl ester **725257-11-4P**, Cyclopropanecarboxylic acid N-[2-[1-[3,4-bis(difluoromethoxy)phenyl]-2-(dimethylcarbamoyl)ethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl]amide **725257-13-6P**, Cyclopropanecarboxylic acid N-[2-[1-[3,4-bis(difluoromethoxy)phenyl]-2-carbamoylethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl]amide **725257-14-7P**, Cyclopropanecarboxylic acid N-[2-[1-[3,4-bis(difluoromethoxy)phenyl]-2-hydroxycarbamoylethyl]-3-oxo-2,3-dihydro-1H-isoindol-4-yl]amide

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(PDE4, TNF-α, and/or MMP inhibitor; preparation of (fluoroalkoxyphenylalkyl)isoindolones as PDE4, TNF-α, and/or MMP inhibitors for treatment of inflammatory diseases, autoimmune diseases, cancer, and pain)

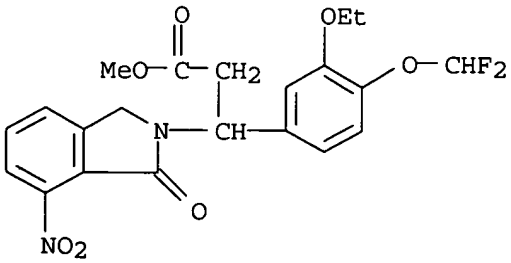
RN 725256-79-1 HCAPLUS

CN 2H-Isoindole-2-propanamide, 7-amino-β-[3-(cyclopropylmethoxy)-4-(difluoromethoxy)phenyl]-1,3-dihydro-N,N-dimethyl-1-oxo- (9CI) (CA INDEX NAME)



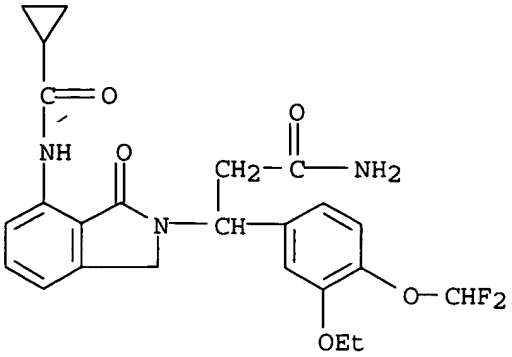
RN 725256-82-6 HCAPLUS

CN 2H-Isoindole-2-propanoic acid, β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-7-nitro-1-oxo-, methyl ester (9CI) (CA INDEX NAME)

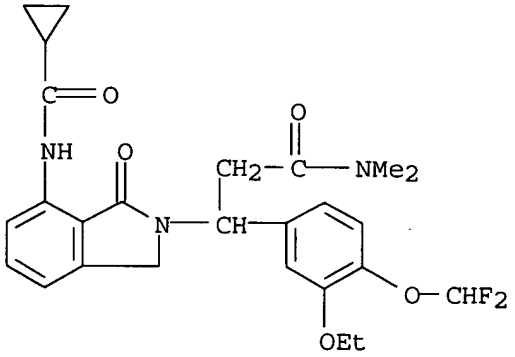


RN 725256-88-2 HCAPLUS

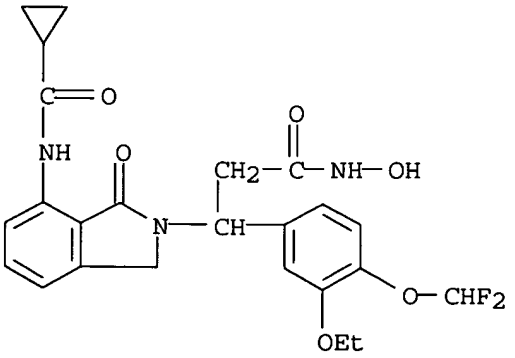
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



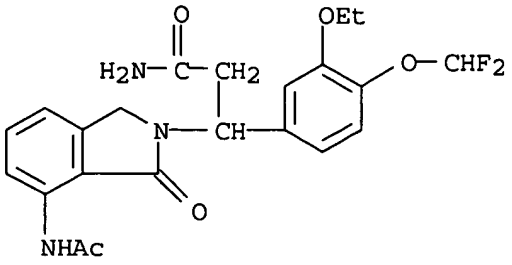
RN 725256-89-3 HCAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-N,N-dimethyl-1-oxo- (9CI) (CA INDEX NAME)



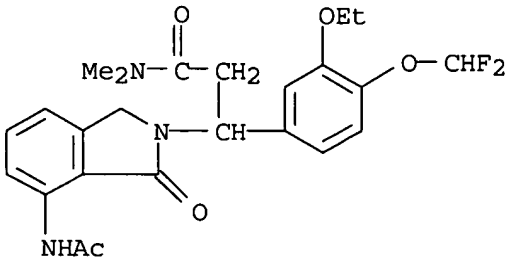
RN 725256-90-6 HCAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-N-hydroxy-1-oxo- (9CI) (CA INDEX NAME)



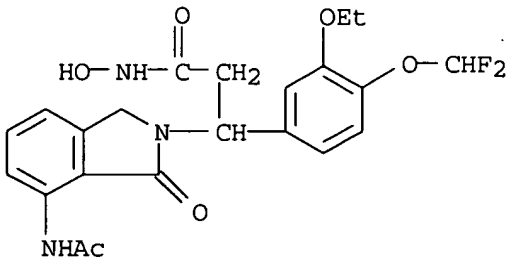
RN 725256-91-7 HCAPLUS
CN 2H-Isoindole-2-propanamide, 7-(acetylamino)-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



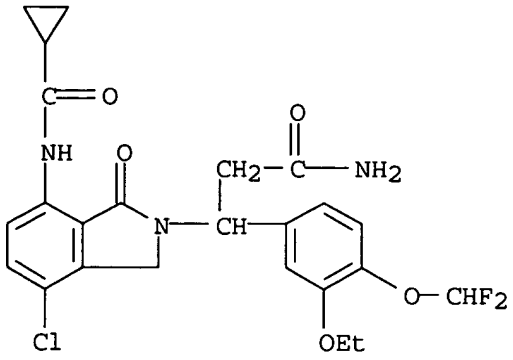
RN 725256-92-8 HCAPLUS
CN 2H-Isoindole-2-propanamide, 7-(acetylamino)-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-N,N-dimethyl-1-oxo- (9CI) (CA INDEX NAME)



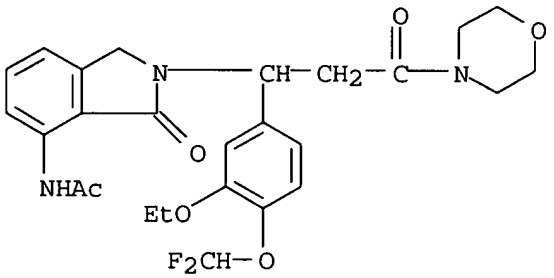
RN 725256-93-9 HCAPLUS
CN 2H-Isoindole-2-propanamide, 7-(acetylamino)-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-N-hydroxy-1-oxo- (9CI) (CA INDEX NAME)



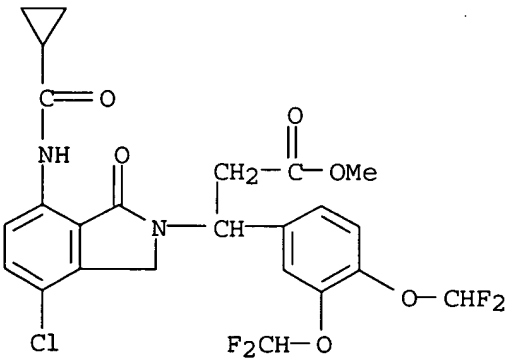
RN 725257-02-3 HCAPLUS
CN 2H-Isoindole-2-propanamide, 4-chloro-7-[(cyclopropylcarbonyl)amino]-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



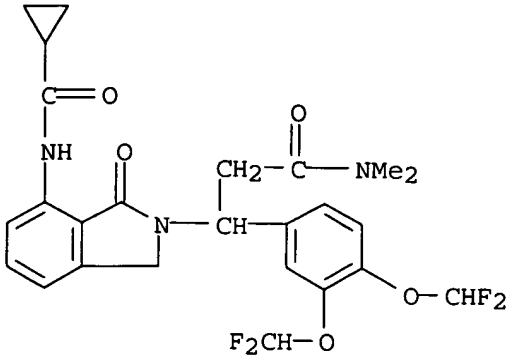
RN 725257-05-6 HCAPLUS
CN Acetamide, N-[2-[1-[4-(difluoromethoxy)-3-ethoxyphenyl]-3-(4-morpholinyl)-3-oxopropyl]-2,3-dihydro-3-oxo-1H-isoindol-4-yl]- (9CI) (CA INDEX NAME)



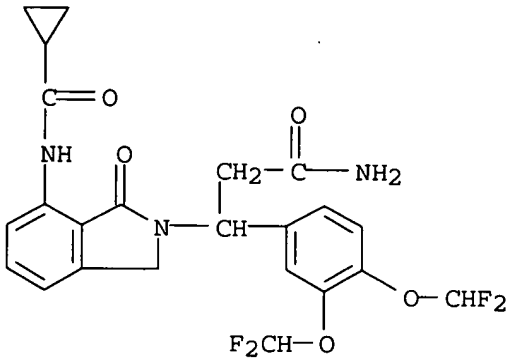
RN 725257-08-9 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-[3,4-bis(difluoromethoxy)phenyl]-4-chloro-7-[(cyclopropylcarbonyl)amino]-1,3-dihydro-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



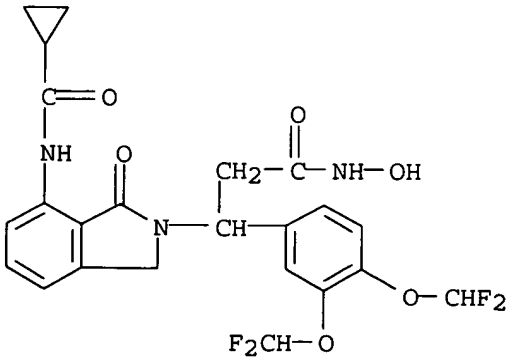
RN 725257-11-4 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-[3,4-bis(difluoromethoxy)phenyl]-7-[(cyclopropylcarbonyl)amino]-1,3-dihydro-N,N-dimethyl-1-oxo- (9CI) (CA INDEX NAME)



RN 725257-13-6 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-[3,4-bis(difluoromethoxy)phenyl]-7-[(cyclopropylcarbonyl)amino]-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



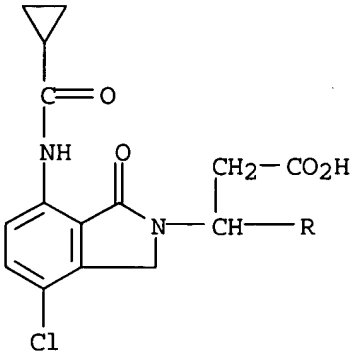
RN 725257-14-7 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-[3,4-bis(difluoromethoxy)phenyl]-7-[(cyclopropylcarbonyl)amino]-1,3-dihydro-N-hydroxy-1-oxo- (9CI) (CA INDEX NAME)

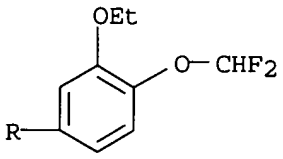


IT **725257-03-4**, 3-[4-Chloro-7-(cyclopropylcarbonylamino)-1-oxo-1,3-dihydroisoindol-2-yl]-3-(4-difluoromethoxy-3-ethoxyphenyl)propionic acid
725257-15-8, 3-[3,4-Bis(difluoromethoxy)phenyl]-3-[7-

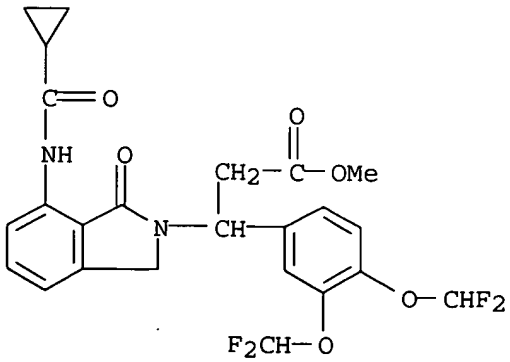
(cyclopropylcarbonylamino)-1-oxo-1,3-dihydroisoindol-2-yl]propionic acid methyl ester
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of (fluoroalkoxyphenylalkyl)isoindolones as PDE4, TNF-α, and/or MMP inhibitors for treatment of inflammatory diseases, autoimmune diseases, cancer, and pain)

RN 725257-03-4 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, 4-chloro-7-[(cyclopropylcarbonyl)amino]-β-[4-(difluoromethoxy)-3-ethoxyphenyl]-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)





RN 725257-15-8 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-[3,4-bis(difluoromethoxy)phenyl]-7-[(cyclopropylcarbonyl)amino]-1,3-dihydro-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



L10 ANSWER 12 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:531300 HCAPLUS
DOCUMENT NUMBER: 141:94292

TITLE: Methods of using and compositions comprising (-)-3-(3,4-dimethoxy-phenyl)-3-(1-oxo-1,3-dihydro-isoindol-2-yl)-propionamide
INVENTOR(S): Muller, George W.; Chen, Roger Shen-chu
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004054501	A2	20040701	WO 2003-US36741	20031117
WO 2004054501	A3	20040826		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2506442	AA	20040701	CA 2003-2506442	20031117
US 2004167199	A1	20040826	US 2003-715184	20031117
EP 1569599	A2	20050907	EP 2003-789795	20031117
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BR 2003016256	A	20051004	BR 2003-16256	20031117
CN 1738614	A	20060222	CN 2003-80108901	20031117

PRIORITY APPLN. INFO.:

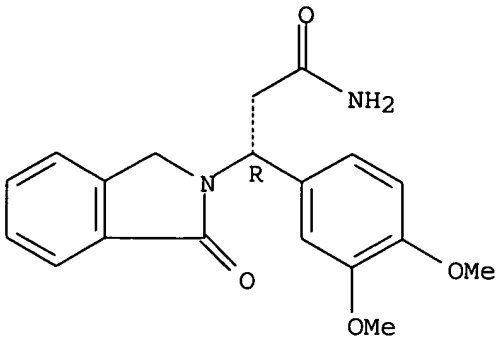
US 2002-427380P	P	20021118
WO 2003-US36741	W	20031117

AB Enantiomerically pure (-)-3-(3,4-dimethoxy-phenyl)-3-(1-oxo-1,3-dihydro-isoindol-2-yl)-propionamide (I), prodrugs, metabolites, polymorphs, salts, solvates, and clathrates thereof are described. Methods of treating and/or preventing various diseases and disorders, such as those ameliorated by the reduction of levels of TNF-α or the inhibition of phosphodiesterase 4 (PDE4), are also disclosed. For example, I gave an TNF-α IC50 of 3 μM and 16 μM in LPS- and IL1β-induced production of TNF-α, resp.,. Also, I showed selectivity for human PDE4 with IC50 of 4.4 μM.

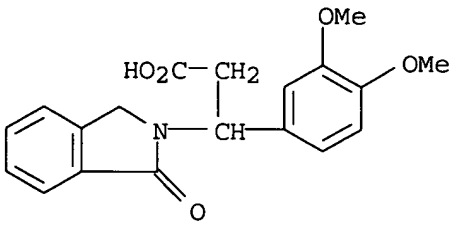
IT **682359-77-9P**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation, compns. and therapeutic uses of (dimethoxyphenyl)-(oxodihydroisoindolyl)propionamide enantiomer as inhibitor of TNFα and PDE4)

RN 682359-77-9 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

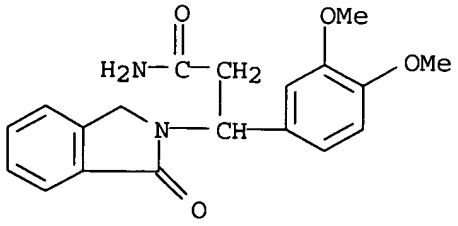
Absolute stereochemistry. Rotation (-).



IT **167886-75-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation, compns. and therapeutic uses of (dimethoxyphenyl)-(oxodihydroisoindolyl)propionamide enantiomer as inhibitor of TNFα and PDE4)
RN 167886-75-1 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)

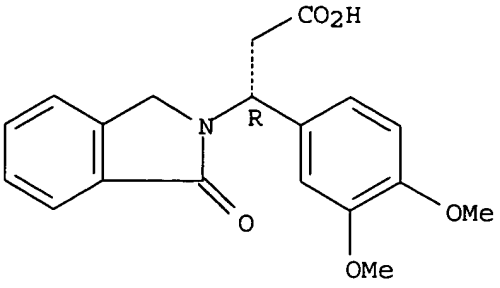


IT **167886-76-2P 713513-04-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, compns. and therapeutic uses of (dimethoxyphenyl)-(oxodihydroisoindolyl)propionamide enantiomer as inhibitor of TNFα and PDE4)
RN 167886-76-2 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



RN 713513-04-3 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 13 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:453020 HCAPLUS
DOCUMENT NUMBER: 141:12309
TITLE: Compositions comprising (+)-3-(3,4-dimethoxyphenyl)-3-(1-oxo-1,3-dihydroisoindol-2-yl)propionamide
INVENTOR(S): Muller, George W.; Chen, Roger Shen-chu
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

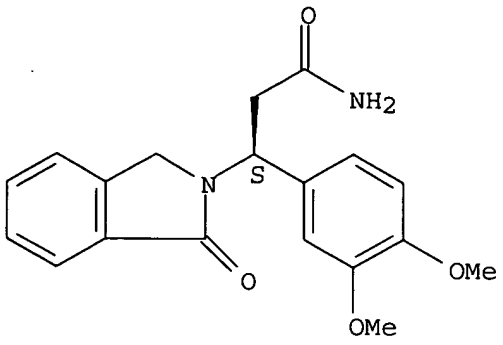
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004045597	A1	20040603	WO 2003-US36740	20031117
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2506232	AA	20040603	CA 2003-2506232	20031117
AU 2003294311	A1	20040615	AU 2003-294311	20031117
BR 2003016259	A	20051004	BR 2003-16259	20031117
EP 1581205	A1	20051005	EP 2003-789794	20031117
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1738613	A	20060222	CN 2003-80108923	20031117
PRIORITY APPLN. INFO.:			US 2002-427379P P	20021118
			WO 2003-US36740 W	20031117

AB Enantiomerically pure (+)-3-(3,4-dimethoxyphenyl)-3-(1-oxo-1,3-dihydroisoindol-2-yl)propionamide (I), and prodrugs, metabolites, polymorphs, salts, solvates (e.g., hydrates), and clathrates are discussed. Methods of treating and/or preventing various diseases and disorders, such as those ameliorated by the reduction of levels of TNF-α or the inhibition of PDE4, are also disclosed. Thus, I was prepared in a series of steps starting from 3,4-dimethoxybenzaldehyde and malonic acid.

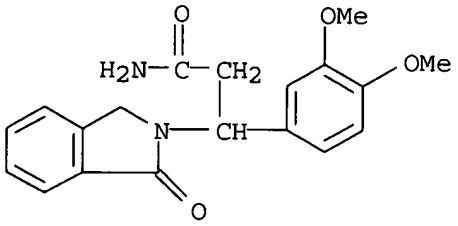
Capsules contained 40.0% I.

IT **682359-78-0P**
RL: PKT (Pharmacokinetics); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(compns. comprising (dimethoxyphenyl)oxodihydroisoindolylpropionamide)
RN 682359-78-0 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo-, (βS)- (9CI) (CA INDEX NAME)

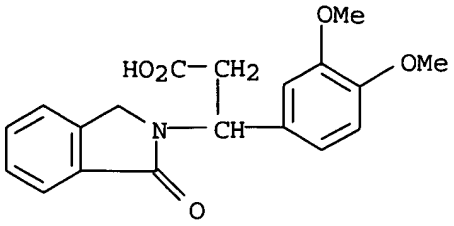
Absolute stereochemistry. Rotation (+).



IT **167886-76-2P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(compns. comprising (dimethoxyphenyl)oxodihydroisoindolylpropionamide)
RN 167886-76-2 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)

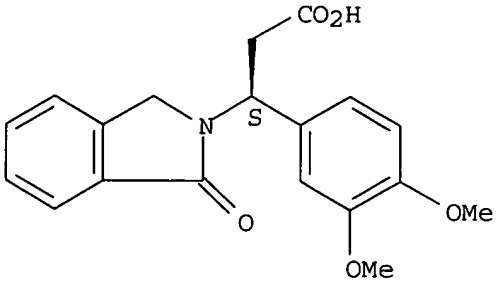


IT **167886-75-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(compns. comprising (dimethoxyphenyl)oxodihydroisoindolylpropionamide)
RN 167886-75-1 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



IT **696641-78-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(compns. comprising (dimethoxyphenyl)oxodihydroisoindolylpropionamide)
RN 696641-78-8 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo-, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L10 ANSWER 14 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:430683 HCAPLUS
DOCUMENT NUMBER: 140:417943
TITLE: Methods of using and compositions comprising selective cytokine inhibitory drugs for the treatment and management of myeloproliferative diseases
INVENTOR(S): Zeldis, Jerome B.
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004043336	A2	20040527	WO 2003-US11325	20030413
WO 2004043336	A3	20040729		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2505003	AA	20040527	CA 2003-2505003		20030413
EP 1569903	A2	20050907	EP 2003-811178		20030413
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003016002	A	20050913	BR 2003-16002		20030413
JP 2006507324	T2	20060302	JP 2004-551394		20030413
PRIORITY APPLN. INFO.:			US 2002-424731P	P	20021106
			WO 2003-US11325	W	20030413

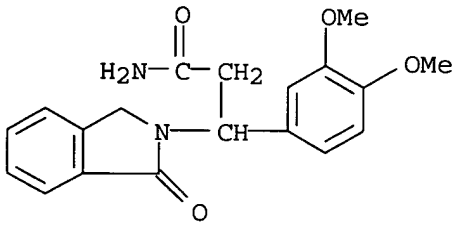
OTHER SOURCE(S): MARPAT 140:417943

AB Methods of treating, preventing and/or managing a myeloproliferative disease (MPD) are disclosed. Specific methods encompass the administration of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in combination with a second active agent, and/or the transplantation of blood or cells. Particular second active agent is capable of suppressing the overprodn. of hematopoietic stem cells or ameliorating one or more of the symptoms of MPD. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed.

IT **167886-76-2**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as selective cytokine inhibitory drug; selective cytokine inhibitory drugs for treatment and management of myeloproliferative diseases)

RN 167886-76-2 HCAPLUS

CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



L10 ANSWER 15 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	2004:428800 HCAPLUS
DOCUMENT NUMBER:	140:417925
TITLE:	Methods and compositions using selective cytokine inhibitory drugs for treatment and management of cancers and other diseases
INVENTOR(S):	Zeldis, Jerome B.
PATENT ASSIGNEE(S):	Celgene Corporation, USA
SOURCE:	PCT Int. Appl., 74 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	5
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004043378	A2	20040527	WO 2003-US35545		20031106
WO 2004043378	A3	20040902			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2505131	AA	20040527	CA 2003-2505131		20031106
EP 1567154	A2	20050831	EP 2003-783234		20031106
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003016057	A	20050920	BR 2003-16057		20031106
CN 1735412	A	20060215	CN 2003-80108390		20031106
US 2006035955	A1	20060216	US 2005-534325		20050912
PRIORITY APPLN. INFO.:			US 2002-424601P	P	20021106
			WO 2003-US35545	W	20031106

OTHER SOURCE(S): MARPAT 140:417925

AB Methods for treating, preventing and/or managing cancer as well as and diseases and disorders associated with, or characterized by, undesired angiogenesis are disclosed. Specific methods encompass the administration of a selective cytokine inhibitory drug alone or in combination with a second active ingredient. The invention further discloses methods for reducing or avoiding adverse side effects associated with chemotherapy, radiation therapy, hormonal therapy, biol. therapy or immunotherapy which comprise the administration of a selective cytokine inhibitory drug. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed.

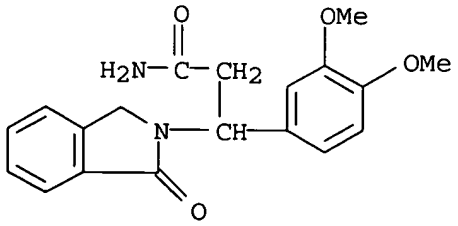
IT **167886-76-2**

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(cytokine inhibitors for treatment and management of cancers and other diseases, and use with other thrapeutic means)

RN 167886-76-2 HCAPLUS

CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



L10 ANSWER 16 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:392056 HCAPLUS

DOCUMENT NUMBER: 140:386062

TITLE: Methods of using and compositions comprising selective

cytokine inhibitory drugs for treatment and management of macular degeneration
INVENTOR(S): Zeldis, Jerome B.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 19 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004091454	A1	20040513	US 2003-699110	20031030
CA 2504263	AA	20040521	CA 2003-2504263	20031031
WO 2004041181	A2	20040521	WO 2003-US34535	20031031
WO 2004041181	A3	20050217		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1567148	A2	20050831	EP 2003-779423	20031031
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003015889	A	20051004	BR 2003-15889	20031031
WO 2005044269	A1	20050519	WO 2004-US13253	20040428
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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.:	US 2002-422900P	P	20021031
	US 2003-699110	A	20031030
	WO 2003-US34535	W	20031031

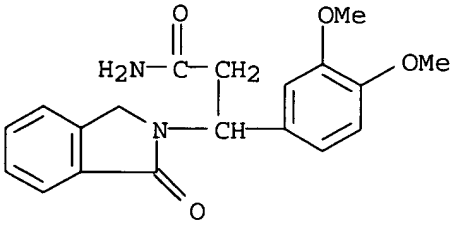
OTHER SOURCE(S): MARPAT 140:386062

AB Methods of treating, preventing and/or managing macular degeneration are disclosed. Specific embodiments encompass the administration of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in combination with a second active agent and/or surgery. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed. Patients with macular degeneration were treated by photodynamic therapy with verteporfin alone, or with the addition of 20 mg/day of selective cytokine inhibitory drug (+)-2-[1-(3-ethoxy-4 methoxyphenyl)-2-methylsulfonylethyl]-4 acetylaminoisoindoline 1,3-dione. The neovascular cascade is sufficiently hindered in the group receiving (+)-2-[1-(3-ethoxy-4 methoxyphenyl)-2-methylsulfonylethyl]-4

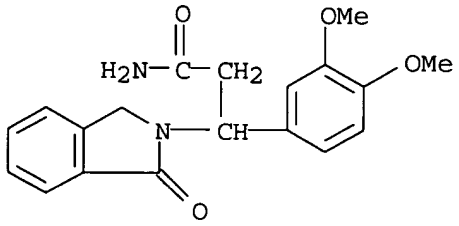
acetylaminoisoindoline 1,3-dione to indefinitely prolong the effects of the photodynamic therapy.

IT **167886-76-2 167886-76-2D**, salts, solvates, stereoisomers
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selective cytokine inhibitory drugs and compns. for treatment and management of macular degeneration)

RN 167886-76-2 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



RN 167886-76-2 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



L10 ANSWER 17 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:372861 HCAPLUS
DOCUMENT NUMBER: 140:368720
TITLE: Compositions comprising selective cytokine inhibitory drugs for treatment, modification and management of pain
INVENTOR(S): Zeldis, Jerome B.; Faleck, Herbert; Manning, Donald C.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 27 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004087558	A1	20040506	US 2003-693722	20031023
PRIORITY APPLN. INFO.:			US 2002-421004P P	20021024

OTHER SOURCE(S): MARPAT 140:368720

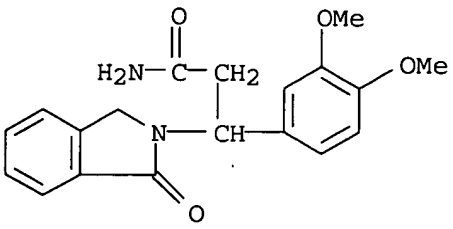
AB Methods of treating, preventing, modifying and managing various types of

pain are disclosed. Specific methods comprise the administration of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in combination with a second active agent and/or surgery, psychol. or phys. therapy. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed. For example, in vitro studies suggested a pharmacol. activity profile for a selective inhibitory drug 3-(3,4-dimethoxyphenyl)-3-(1-oxo-1,3-dihydroisoindol-2-yl)propionamide (I) was 5 to 50 times more potent than thalidomide. The pharmacol. effects of I may derive from its action as an inhibitor of the generation of inflammatory cytokines. The cardiovascular and respiratory changes induced by three ascending doses of I (400, 800, and 1200 mg/kg/day) in dogs were minimal when compared to the vehicle control group.

IT **167886-76-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(selective cytokine inhibitors for treatment, modification and management of pain)

RN 167886-76-2 HCAPLUS

CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



L10 ANSWER 18 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:368895 HCAPLUS

DOCUMENT NUMBER: 140:368714

TITLE: Methods and compositions using selective cytokine inhibitory drugs, alone or in combination with other therapeutic means, for treatment, modification and management of pain

INVENTOR(S): Zeldis, Jerome B.; Faleck, Herbert; Manning, Donald C.

PATENT ASSIGNEE(S): Celgene Corporation, USA

SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004037207	A2	20040506	WO 2003-US334005	20031024
WO 2004037207	A3	20050210		

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OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2503054	AA	20040506	CA 2003-2503054		20031024
EP 1562586	A2	20050817	EP 2003-779299		20031024
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BR 2003015593	A	20050906	BR 2003-15593		20031024
JP 2006505591	T2	20060216	JP 2004-547196		20031024
PRIORITY APPLN. INFO.:			US 2002-421004P	P	20021024
			WO 2003-US34005	W	20031024

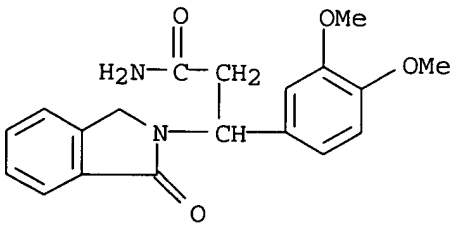
OTHER SOURCE(S): MARPAT 140:368714

AB Methods of treating, preventing, modifying and managing various types of pain are disclosed. Specific methods comprise the administration of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in combination with a second active agent and/or surgery, psychol. or phys. therapy. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed.

IT **167886-76-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cytokine inhibitors, alone or in combination with other therapeutic means, for treatment of pain)

RN 167886-76-2 HCAPLUS

CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



L10 ANSWER 19 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	2004:354722 HCAPLUS
DOCUMENT NUMBER:	140:350585
TITLE:	Treatment and management of myelodysplastic syndromes by administration of selective cytokine inhibitory drugs, and pharmaceutical compositions
INVENTOR(S):	Zeldis, Jerome B.
PATENT ASSIGNEE(S):	Celgene Corporation, USA
SOURCE:	PCT Int. Appl., 50 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

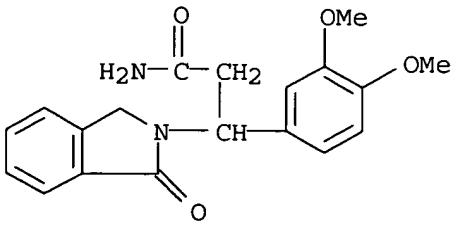
WO 2004034962	A2	20040429	WO 2003-US11324	20030413
WO 2004034962	A3	20040805		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2501936	AA	20040429	CA 2003-2501936	20030413
EP 1551385	A2	20050713	EP 2003-726263	20030413
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
BR 2003015316	A	20050816	BR 2003-15316	20030413
PRIORITY APPLN. INFO.:			US 2002-418470P	P 20021015
			WO 2003-US11324	W 20030413

OTHER SOURCE(S): MARPAT 140:350585

AB The invention discloses methods of treating, preventing and/or managing a myelodysplastic syndrome. Specific methods encompass the administration of a selective cytokine inhibitory drug, or a pharmaceutically acceptable salt, solvate, hydrate, stereoisomer, clathrate, or prodrug thereof, alone or in combination with a second active ingredient, and/or blood or cells for transplantation therapy. The invention also describes the use of such drugs alone or in combination with conventional therapy for myelodysplastic syndromes and/or with transplantation therapy. Specific second active ingredients are capable of affecting or improving blood cell production Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed.

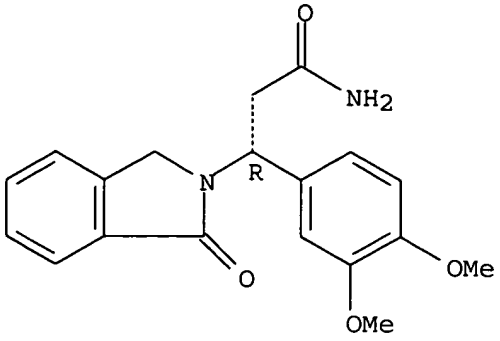
IT **167886-76-2 682359-77-9 682359-78-0**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment and management of myelodysplastic syndromes by administration of selective cytokine inhibitory drugs, and pharmaceutical compns.)

RN 167886-76-2 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



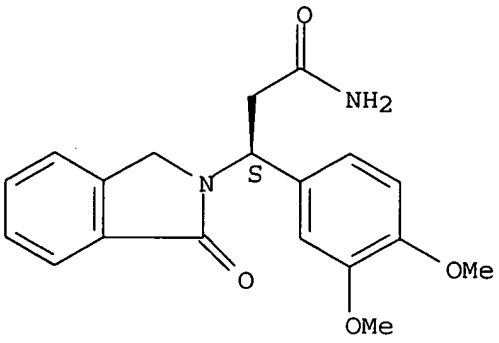
RN 682359-77-9 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 682359-78-0 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo-, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L10 ANSWER 20 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:1001604 HCAPLUS
DOCUMENT NUMBER: 140:42030
TITLE: Preparation of isoindolinediones as angiogenesis inhibitors.
INVENTOR(S): Man, Hon-wah; Muller, George W.
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: U.S., 28 pp., Cont.-in-part of U.S. Ser. No. 590,344.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6667316	B1	20031223	US 2000-708199	20001108
CA 2392081	AA	20010517	CA 2000-2392081	20001109
WO 2001034606	A1	20010517	WO 2000-US30770	20001109

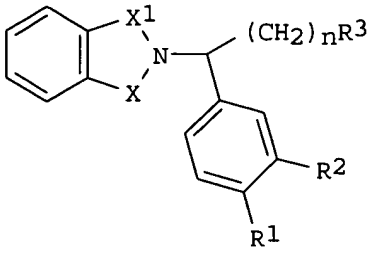
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,

YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1228071	A1	20020807	EP 2000-977095		20001109
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
NZ 519459	A	20031128	NZ 2000-519459		20001109
JP 2004500346	T2	20040108	JP 2001-536553		20001109
AU 782409	B2	20050728	AU 2001-14780		20001109
NO 2002002223	A	20020708	NO 2002-2223		20020508
FI 2002000892	A	20020510	FI 2002-892		20020510
US 2004147588	A1	20040729	US 2003-685942		20031014
PRIORITY APPLN. INFO.:			US 1999-165168P	P	19991112
			US 2000-590344	A2	20000608
			US 2000-708199	A	20001108
			WO 2000-US30770	W	20001109

OTHER SOURCE(S): MARPAT 140:42030

GI



I

AB Title compds. [I; R1, R2 = alkyl, alkoxy, cyano, cycloalkoxy, cycloalkyl, cycloalkylmethoxy; 1 of X and X1 = CO, SO2 and the other of X and X1 = CO, CH2, SO2, CH2CO; R3 = SO2Y, COZ, CN, hydroxyalkyl; Y = alkyl, Ph, PhCH2; Z = NR61R71, alkyl, Ph, PhCH2; R61 = H, alkyl, cycloalkyl, Ph, PhCH2, etc.; R71 = alkyl; 1 of R4, R5 = H and the other = imidazolyl, pyrrolyl, oxadiazolyl, triazolyl, R6R7N(CzH2z); z = 0, 1; n = 1-3; R6 = cycloalkanoyl which is unsubstituted or substituted with halo, amino, monoalkylamino, dialkylamino; R4R5 = NHCH2R8, NHCOR8, N:CHR8; R7 = H, alkyl, methylsulfonyl, alkoxyalkylcarbonyl; R8 = CH2, O, NH, CH:CH, CH:N], were prepared for treatment of undesirable angiogenesis (no data). Thus, 3,4-dinitrophthalic acid and 2-(3-ethoxy-4-methoxyphenyl)-1-(methylsulfonyl)eth-2-ylamine in PhMe were refluxed for 15 h through a Dean-Stark trap to give 49% 2-[1-(3-Ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4,5-dinitroisoindoline-1,3-dione. This was hydrogenated in EtOAc over Pd/C to give 73% 2-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-4,5-diaminoisoindoline-1,3-dione. The latter was refluxed 17 h with DMF di-Me acetal in HOAc to give 68% 7-[1-(3-ethoxy-4-methoxyphenyl)-2-methylsulfonylethyl]-3-pyrrolino[3,4-e]benzimidazole-6,8-dione.

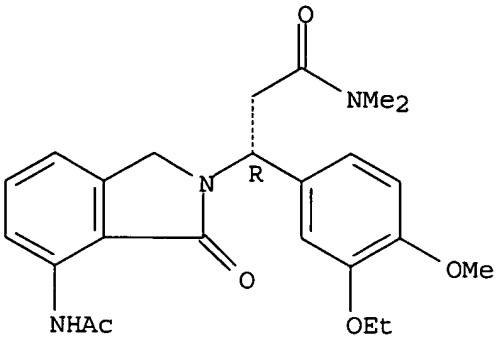
IT **340019-71-8P 340019-72-9P 635705-68-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of isoindolinediones as angiogenesis inhibitors)

RN 340019-71-8 HCAPLUS

CN 2H-Isoindole-2-propanamide, 7-(acetylamino)-β-(3-ethoxy-4-

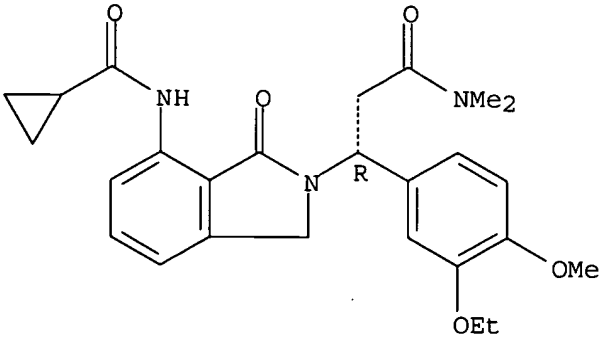
methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



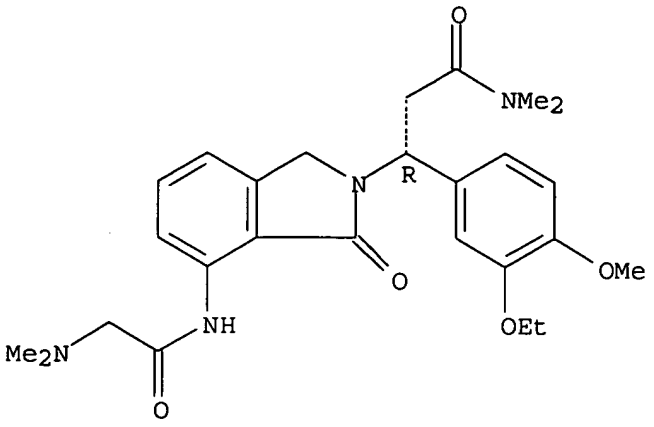
RN 340019-72-9 HCAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



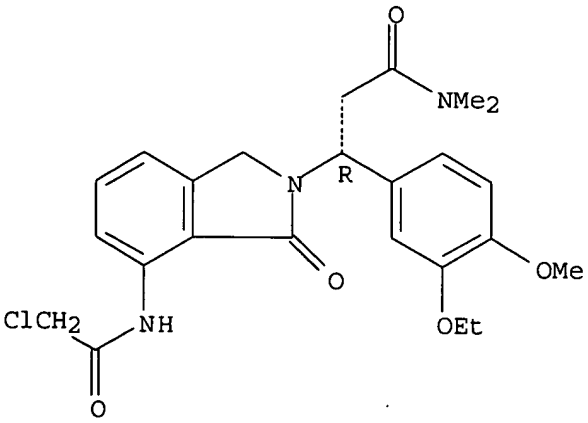
RN 635705-68-9 HCAPLUS
CN 2H-Isoindole-2-propanamide, 7-[[(dimethylamino)acetyl]amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



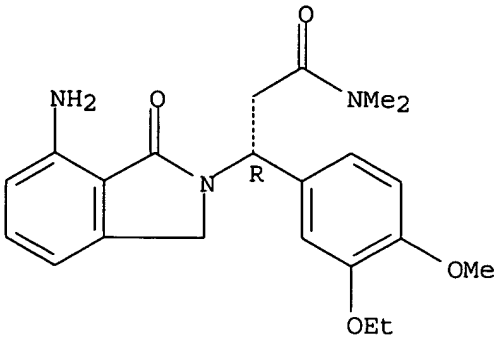
IT **340019-74-1 340020-04-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of isoindolinediones as angiogenesis inhibitors)
RN 340019-74-1 HCAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(chloroacetyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 340020-04-4 HCAPLUS
CN 2H-Isoindole-2-propanamide, 7-amino-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 21 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:931165 HCAPLUS
DOCUMENT NUMBER: 139:391341
TITLE: Methods and compositions using selective cytokine inhibitory drugs for treatment and management of cancers and other diseases
INVENTOR(S): Zeldis, Jerome B.
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003097040	A1	20031127	WO 2003-US315468		20030516
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2486141	AA	20031127	CA 2003-2486141		20030516
AU 2003234624	A1	20031202	AU 2003-234624		20030516
EP 1556033	A1	20050727	EP 2003-728967		20030516
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP 2005530780	T2	20051013	JP 2004-505039		20030516
US 2005234017	A1	20051020	US 2005-515270		20050523
PRIORITY APPLN. INFO.:			US 2002-380842P	P	20020517
			US 2002-424601P	P	20021106
			WO 2003-US15468	W	20030516

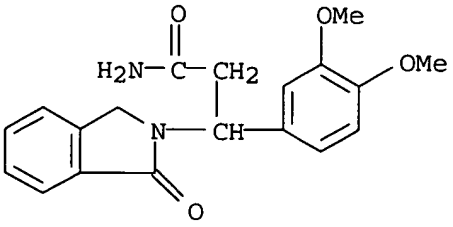
OTHER SOURCE(S): MARPAT 139:391341
AB Methods of treating, preventing and/or managing cancer as well as and diseases and disorders associated with, or characterized by, undesired

angiogenesis are disclosed. Specific methods encompass the administration of a selective cytokine inhibitory drug alone or in combination with a second active ingredient. The invention further relates to methods of reducing or avoiding adverse side effects associated with chemotherapy, radiation therapy, hormonal therapy, biol. therapy or immunotherapy which comprise the administration of a selective cytokine inhibitory drug. Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed.

IT **167886-76-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. using selective cytokine inhibitory drugs for treatment and management of cancers and other diseases)

RN 167886-76-2 HCAPLUS

CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 22 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:835303 HCAPLUS

DOCUMENT NUMBER: 138:378817

TITLE: Thalidomide and its analogues have distinct and opposing effects on TNF-α and TNFR2 during co-stimulation of both CD4+ and CD8+ T cells

AUTHOR(S): Marriott, J. B.; Clarke, I. A.; Dredge, K.; Muller, G.; Stirling, D.; Dalgleish, A. G.

CORPORATE SOURCE: Division of Oncology, Department of OGEM, St George's Hospital Medical School, London, UK

SOURCE: Clinical and Experimental Immunology (2002), 130(1), 75-84
CODEN: CEXIAL; ISSN: 0009-9104

PUBLISHER: Blackwell Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

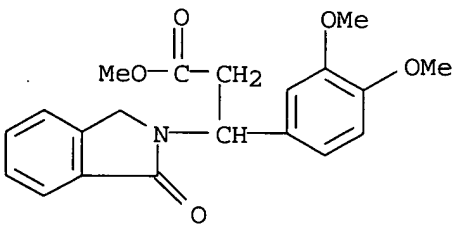
AB Thalidomide (Thd) is clin. useful in a number of conditions where its efficacy is probably related to its anti-TNF-α activity. More recently, Thd has also been shown to co-stimulate T cells and second generation co-stimulatory (IMiD) analogs are currently being assessed in the treatment of cancer patients. However, in contrast to their known suppressive effects during inflammatory stimuli, the effects of Thd/IMiDs on TNF-α and TNF receptors (TNFRs) during T cell co-stimulation are not known. We sought to determine the effect of Thd, two clin. relevant IMiDs (CC-4047, ACTIMID and CC-5013, REVIMID) and a non-stimulatory SelCID analog (CC-3052) on TNF-α production and on the expression and shedding of TNFRs during co-stimulation. We found that co-stimulation of PBMC with Thd/IMiDs, but not CC-3052, prevented αCD3-induced T cell surface

expression of TNFR2 and thereby reduced soluble TNFR2 (sTNFR2) levels. However, there was no effect on total (surface/intracellular) TNFR2 protein expression, suggesting inhibition of trafficking to the cell membrane. The extent of co-stimulation by Thd/IMiDs (assessed by CD69/CD25 expression and IL-2/sIL-2R a production) was similar for CD4+ and CD8+ T lymphocytes and correlated with TNFR2 inhibition. Co-stimulation, but not the early inhibitory effect on TNFR2, was IL-2-dependent and led to increased TNF-α production by both CD4+ and CD8+ T lymphocytes. The clin. relevance of this observation was confirmed by the elevation of serum TNF-α during REVIMID treatment of patients with advanced cancer. Together, these results suggest a possible role for TNF-mediated events during co-stimulation and contrast with the TNF inhibitory effects of Thd and its analogs during inflammatory stimuli.

IT **216884-02-5**, CC 3052
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); BIOL (Biological study)
(thalidomide and its analogs distinct and opposing effects on TNF-α and TNFR2 during co-stimulation of CD4+ and CD8+ T cells)

RN 216884-02-5 HCAPLUS

CN 2H-Isoindole-2-propanoic acid, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 23 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:472708 HCAPLUS
DOCUMENT NUMBER: 135:76876
TITLE: Preparation of 2-(1,3,4-oxadiazol-2-yl)ethylisoindoline-1,3-diones as phosphodiesterase 4 inhibitors which decrease tumor necrosis factor-α levels
INVENTOR(S): Man, Hon-Wah; Muller, George
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001046183	A1	20010628	WO 2000-US34457	20001219

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,

SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6326388	B1	20011204	US 1999-470203	19991221
CA 2394615	AA	20010628	CA 2000-2394615	20001219
EP 1242413	A1	20020925	EP 2000-986568	20001219
EP 1242413	B1	20041117		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003518115	T2	20030603	JP 2001-547093	20001219
EP 1462449	A1	20040929	EP 2004-3830	20001219
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AT 282612	E	20041215	AT 2000-986568	20001219
EP 1510518	A2	20050302	EP 2004-20108	20001219
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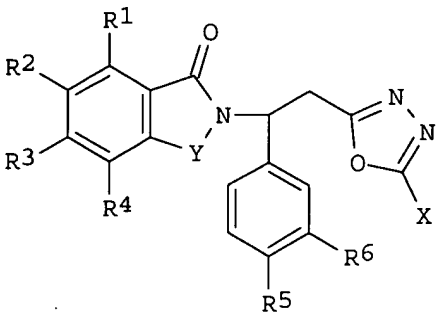
PT 1242413	T	20050331	PT 2000-986568	20001219
ES 2233488	T3	20050616	ES 2000-986568	20001219
AU 782168	B2	20050707	AU 2001-22785	20001219
NO 2002002937	A	20020815	NO 2002-2937	20020618
FI 2002001192	A	20020619	FI 2002-1192	20020619
HK 1050522	A1	20050902	HK 2003-101117	20030217
PRIORITY APPLN. INFO.:			US 1999-470203 A	19991221
			EP 2000-986568 A3	20001219
			WO 2000-US34457 W	20001219

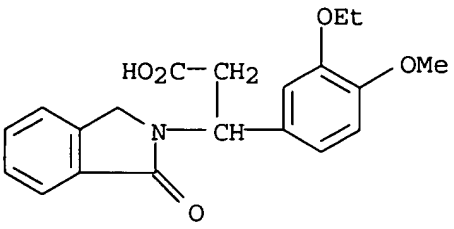
OTHER SOURCE(S): MARPAT 135:76876
GI



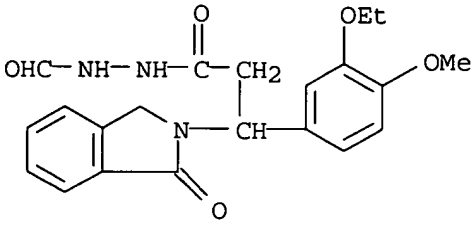
I

AB Title compds. (I; Y = CO, CH2, SO2, CH2CO; X = H, alkyl; R1-R4 = H, halo, CF3, Ac, alkyl, alkoxy, NO2, cyano, OH, CMe3, etc.; adjacent R1-R4 = atoms to form with the Ph ring a naphthylidene, quinoline, quinoxaline, benzimidazole, benzodioxole, or 2-hydroxybenzimidazole ring; R5, R6 = H, alkyl, alkoxy, cyano, benzocycloalkoxy, cycloalkoxy, etc.), were prepared for treatment of inflammation, autoimmune disease, and cancer (no data). Thus, 3-(3-cyclopentyloxy-4-methoxyphenyl)-3-(5-methyl-1,3-dioxoisoindolin-2-yl)propanoic acid, carbonyldiimidazole, and formic hydrazide were stirred in EtOAc to give crude N-carbonylamino-3-(3-cyclopentyloxy-4-methoxyphenyl)-3-(5-methyl-1,3-dioxoisoindolin-2-yl)propanamide, which was treated with POCl3 in MeCN to give 32% 2-[1-(3-cyclopentyloxy-4-methoxyphenyl)-2-(1,3,4-oxadiazol-2-yl)ethyl]-5-methylisoindoline-1,3-dione. Drug formulations containing the latter are given.

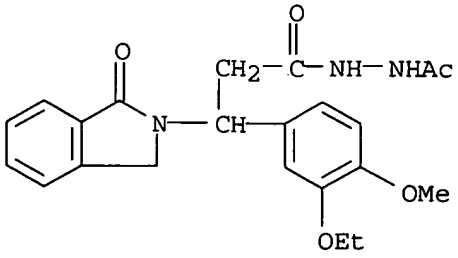
IT **200483-25-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of oxadiazolylethylisoindolinediones as phosphodiesterase 4 inhibitors which decrease tumor necrosis factor-α levels)
RN 200483-25-6 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



IT **347192-09-0P 347192-10-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of oxadiazolylethylisoindolinediones as phosphodiesterase 4 inhibitors which decrease tumor necrosis factor-α levels)
RN 347192-09-0 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, 2-formylhydrazide (9CI) (CA INDEX NAME)



RN 347192-10-3 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, 2-acetylhydrazide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

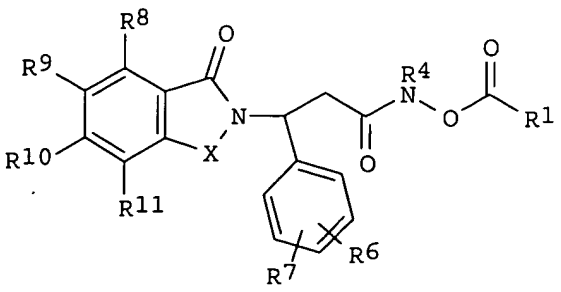
L10 ANSWER 24 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:472490 HCAPLUS
DOCUMENT NUMBER: 135:76791
TITLE: Preparation of 1,3-dioxoisoindolin-2-yl-N-acyloxypropanamides as phosphodiesterase 4 inhibitors which reduce undesirable levels of tumor necrosis factor-α.
INVENTOR(S): Man, Hon-Wah; Muller, George; Huang, Shaei Y.
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001045702	A1	20010628	WO 2000-US34455	20001219
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6699899	B1	20040302	US 1999-468529	19991221
CA 2394604	AA	20010628	CA 2000-2394604	20001219
EP 1246620	A1	20021009	EP 2000-988151	20001219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003518060	T2	20030603	JP 2001-546641	20001219
NZ 519638	A	20030926	NZ 2000-519638	20001219
AU 782634	B2	20050818	AU 2001-24389	20001219
NO 2002002936	A	20020814	NO 2002-2936	20020618
FI 2002001193	A	20020731	FI 2002-1193	20020619
US 2004167174	A1	20040826	US 2004-786822	20040225

PRIORITY APPLN. INFO.: US 1999-468529 A 19991221
WO 2000-US34455 W 20001219

OTHER SOURCE(S): MARPAT 135:76791
GI

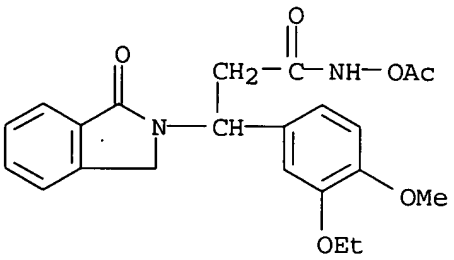


I

AB Title compds. (I; R4 = H, COR12; R1, R12 = alkyl, Ph, PhCH2, pyridyl, pyridylmethyl, imidazolyl, imidazolylmethyl, etc.; X = CO, CH2, CH2CO, SO2; R6, R7 = NO2, cyano, CF3, EtO2C, Ac, AcO, CO2H, OH, amino, etc.; R8-R11 = H, NO2, cyano, CF3, EtO2C, MeO2C, Ac, carbamoyl, AcO, CO2H, amino, acylamino, etc.; or R8R9, R10R11 = benzo, quinolino, quinoxalino, etc.; R9R10 = benzo), were prepared as drugs (no data). Thus, 3-(1,3-dioxoisoindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propanehydroxamic acid was stirred with propionic anhydride in MeCN overnight to give [3-(1,3-dioxoisoindolin-2-yl)-3-(3-ethoxy-4-methoxyphenyl)propanoylamino]propanoate. Drug formulations containing the latter were given.

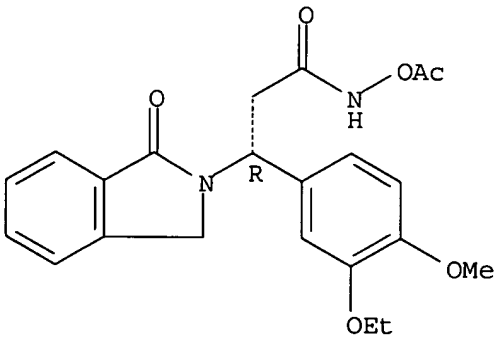
IT **347144-62-1P 347144-63-2P 347144-64-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1,3-dioxoisoindolin-2-yl-N-acyloxypropanamides as phosphodiesterase 4 inhibitors which reduce undesirable levels of tumor necrosis factor-α)

RN 347144-62-1 HCAPLUS
CN 2H-Isoindole-2-propanamide, N-(acetyloxy)-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



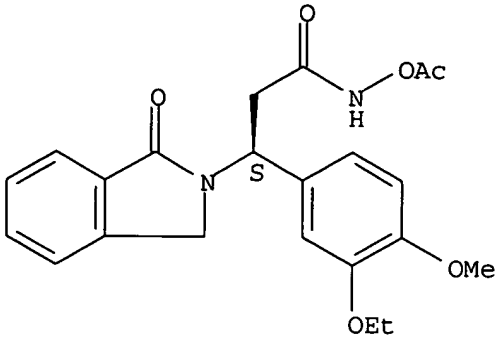
RN 347144-63-2 HCAPLUS
CN 2H-Isoindole-2-propanamide, N-(acetyloxy)-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

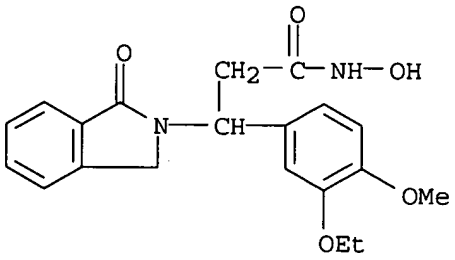


RN 347144-64-3 HCAPLUS
CN 2H-Isoindole-2-propanamide, N-(acetyloxy)-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, (βS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **220360-64-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 1,3-dioxoisoindolin-2-yl-N-acyloxypropanamides as phosphodiesterase 4 inhibitors which reduce undesirable levels of tumor necrosis factor-α)
RN 220360-64-5 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N-hydroxy-1-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 25 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:452859 HCAPLUS
DOCUMENT NUMBER: 135:51096
TITLE: Compositions for the prevention and treatment of atherosclerosis and restenosis
INVENTOR(S): Zeldis, Jerome B.
PATENT ASSIGNEE(S): Celgene Corp., USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001043743	A1	20010621	WO 2000-US33708	20001213

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,

SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

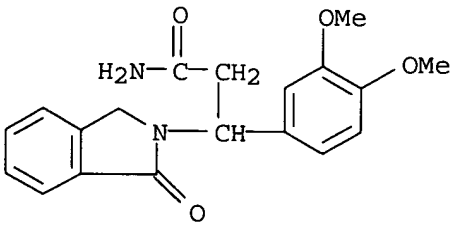
US 2002054899	A1	20020509	US 2000-734460	20001211
CA 2395474	AA	20010621	CA 2000-2395474	20001213
AU 2001020916	A5	20010625	AU 2001-20916	20001213
AU 782753	B2	20050825		
EP 1242082	A1	20020925	EP 2000-984269	20001213
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003517012	T2	20030520	JP 2001-544881	20001213
US 2006004054	A1	20060105	US 2005-216950	20050830
PRIORITY APPLN. INFO.:			US 1999-170820P	P 19991215
			US 2000-734460	A3 20001211
			WO 2000-US33708	W 20001213

AB Methods and compns. for the prevention and treatment of all forms of atherosclerosis are described. Administration of compds. such as thalidomide, its analogs, hydrolysis products, metabolites, derivs. and precursors as well as addnl. compds. capable of inhibiting tumor necrosis factor-α (TNF-α) are used in the invention. Also disclosed is the coating of prosthetic devices, such as stents, with the compds. of the invention for the prevention and/or treatment of restenosis. Tablets contained 1-oxo-2-(2,6-dioxopiperidin-3-yl)-4-aminoisoindoline 50.0, lactose 50.7, wheat starch 7.5, PEG-6000 5.0, talc 5.0, and Mg stearate 1.8 and water qs.

IT **167886-76-2**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (compns. for prevention and treatment of atherosclerosis and restenosis)

RN 167886-76-2 HCAPLUS

CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

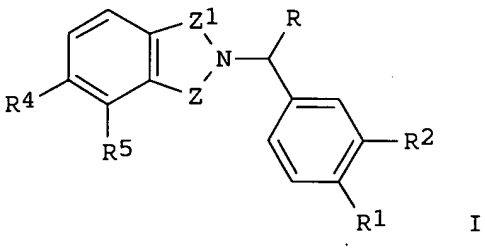
L10 ANSWER 26 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	2001:359998 HCAPLUS
DOCUMENT NUMBER:	134:366799
TITLE:	Preparation of isoindolinones for treatment of phosphodiesterase- and TNFα-mediated diseases
INVENTOR(S):	Man, Hon-Wah; Muller, George
PATENT ASSIGNEE(S):	Celgene Corporation, USA
SOURCE:	PCT Int. Appl., 94 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034606	A1	20010517	WO 2000-US30770	20001109
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6667316	B1	20031223	US 2000-708199	20001108
CA 2392081	AA	20010517	CA 2000-2392081	20001109
EP 1228071	A1	20020807	EP 2000-977095	20001109
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NZ 519459	A	20031128	NZ 2000-519459	20001109
JP 2004500346	T2	20040108	JP 2001-536553	20001109
AU 782409	B2	20050728	AU 2001-14780	20001109
NO 2002002223	A	20020708	NO 2002-2223	20020508
FI 2002000892	A	20020510	FI 2002-892	20020510
PRIORITY APPLN. INFO.:			US 1999-165168P P	19991112
			US 2000-590344 A	20000608
			US 2000-708199 A	20001108
			WO 2000-US30770 W	20001109

OTHER SOURCE(S): MARPAT 134:366799
GI



I

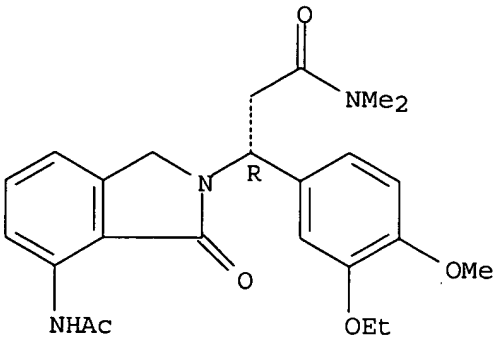
AB Title compds. [I; R = (CnH2n)R3; R1,R2 = (cyclo)alkyl(oxy), cyano, cycloalkylmethoxy; R3 = hydroxyalkyl, cyano, SO2R6, COR7; 1 of R4,R5 = H and the other = pyrrolyl, imidazolyl, (un)substituted amino(alkyl), etc.; R4,R5 = (un)substituted amino(alkyl); R4R5 = atoms to complete a ring; R6 = alkyl, Ph, CH2Ph; R7 = groups cited for R6, (un)substituted amino; 1 of Z,Z1 = CO or SO2 and the other = CH2, CO, SO2, CH2CO; n = 1-3] were prepared for treatment of phosphodiesterase- and TNFα-mediated diseases (no data). Thus, 3,4-dinitrophthalic acid was cyclocondensed with H2NCH(CH2SO2Me)C6H3(OEt)(OMe)-3,4 and the product reduced to give I (R = CH2SO2Me, R1 = OMe, R2 = OEt, R4 = R5 = NH2, Z = Z1 = CO).

IT **340019-71-8P 340019-72-9P 340019-74-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of isoindolinones for treatment of phosphodiesterase- and TNFα-mediated diseases)

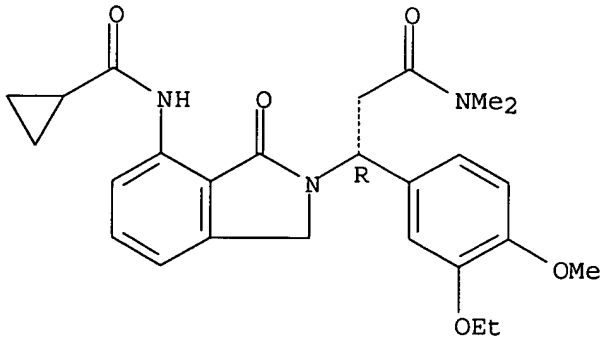
RN 340019-71-8 HCAPLUS
CN 2H-Isoindole-2-propanamide, 7-(acetylamino)-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



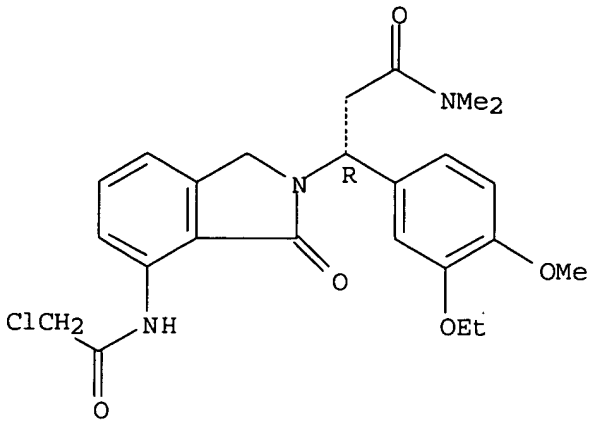
RN 340019-72-9 HCAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(cyclopropylcarbonyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



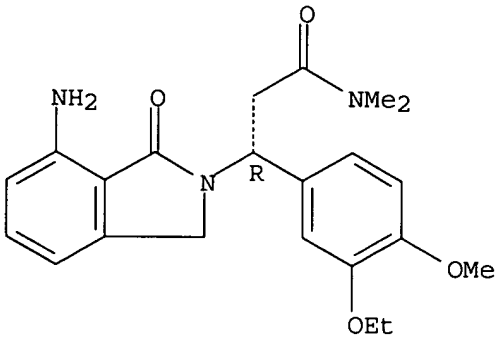
RN 340019-74-1 HCAPLUS
CN 2H-Isoindole-2-propanamide, 7-[(chloroacetyl)amino]-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **340020-04-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of isoindolinones for treatment of phosphodiesterase- and TNFα-mediated diseases)
RN 340020-04-4 HCAPLUS
CN 2H-Isoindole-2-propanamide, 7-amino-β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N,N-dimethyl-1-oxo-, (βR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

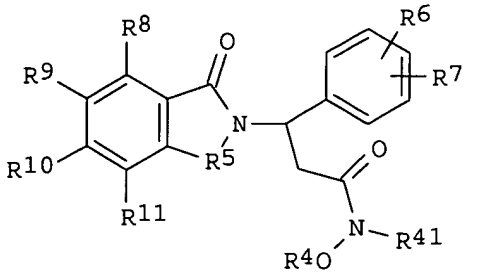


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 27 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:255928 HCAPLUS
DOCUMENT NUMBER: 134:280706
TITLE: Preparation of isoindolylhydroxypropionamides for reduction of tumor necrosis factor-α levels.
INVENTOR(S): Muller, George W.; Man, Hon-Wah
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: U.S., 17 pp., Cont.-in-part of U.S. Ser. No. 903,975, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6214857	B1	20010410	US 1998-126157	19980730
TR 200000221	T2	20000921	TR 2000-200000221	19980730
PT 1035848	T	20030930	PT 1998-938151	19980730
ES 2196592	T3	20031216	ES 1998-938151	19980730
MX 200001018	A	20001110	MX 2000-1018	20000128
US 2001049371	A1	20011206	US 2001-780725	20010209
US 6656964	B2	20031202		
US 2004006096	A1	20040108	US 2003-462319	20030616
PRIORITY APPLN. INFO.:			US 1997-903975 B2	19970731
			US 1998-126157 A3	19980730
			US 2000-590344 A3	20000608
			US 2001-780725 A1	20010209

OTHER SOURCE(S): MARPAT 134:280706
GI



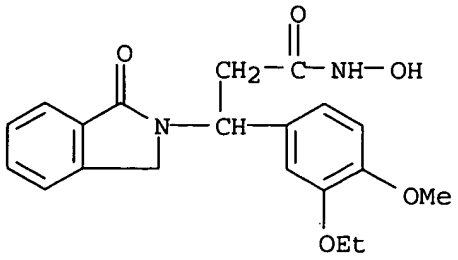
I

AB Title compds. e.g., (I; R4, R41 = H, alkyl; R5 = CO, CH2; R6, R7 = NO2, cyano, CF3, EtO2C, MeO2C, Ac, AcO, CO2H, OH, alkyl, etc.; R8-R11 = H, NO2, cyano, CF3, EtO2C, MeO2C, Ac, AcO, CO2H, OH, amino, acylamino, alkyl, etc.), were prepared for reduction of TNF-α levels (no data). Thus, 3-(3-ethoxy-4-methoxyphenyl)-3-(1-oxoisoindolinyl)propanoic acid and carbonyldiimidazole were stirred 2 h in THF; NH2OH.HCl was added and the resulting suspension was stirred 18 h to give 82% 3-(3-ethoxy-4-methoxyphenyl)-N-hydroxy-3-(1-oxoisoindolinyl)propionamide. I drug formulations are given.

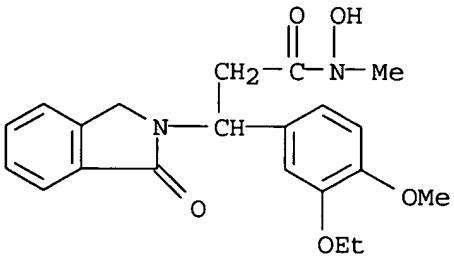
IT **220360-64-5P 220360-68-9P 220360-70-3P**
220360-73-6P 220360-80-5P 220360-81-6P
220360-84-9P 333366-51-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of isoindolylhydroxypropionamides for reduction of tumor necrosis factor-α levels)

RN 220360-64-5 HCAPLUS

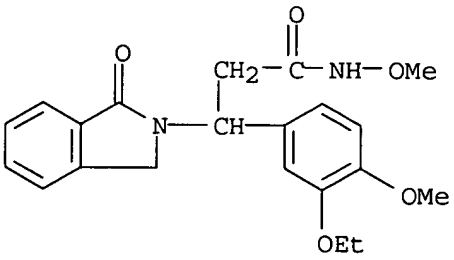
CN 2H-Isoindole-2-propanamide, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N-hydroxy-1-oxo- (9CI) (CA INDEX NAME)



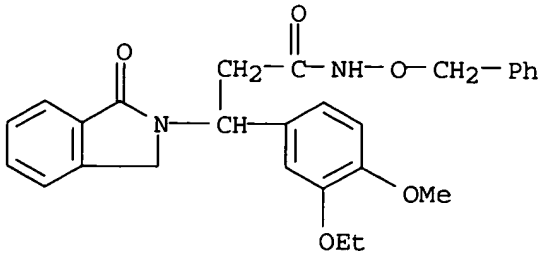
RN 220360-68-9 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N-hydroxy-N-methyl-1-oxo- (9CI) (CA INDEX NAME)



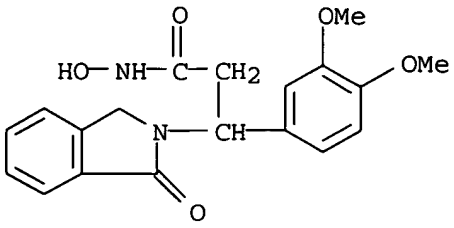
RN 220360-70-3 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N-methoxy-1-oxo- (9CI) (CA INDEX NAME)



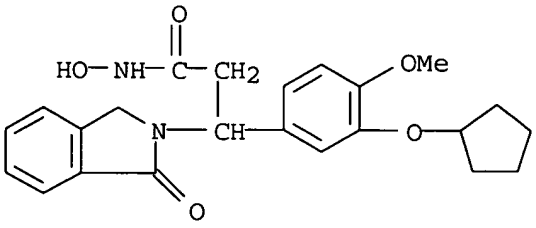
RN 220360-73-6 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-N-(phenylmethoxy)- (9CI) (CA INDEX NAME)



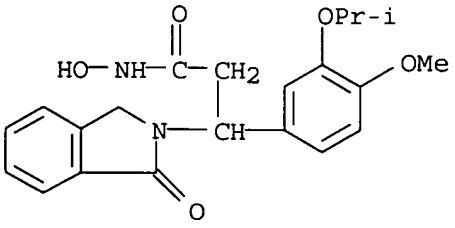
RN 220360-80-5 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-N-hydroxy-1-oxo- (9CI) (CA INDEX NAME)



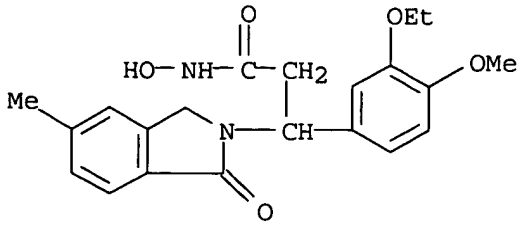
RN 220360-81-6 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,3-dihydro-N-hydroxy-1-oxo- (9CI) (CA INDEX NAME)



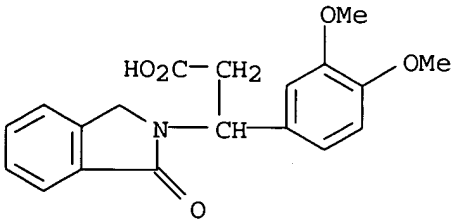
RN 220360-84-9 HCAPLUS
CN 2H-Isoindole-2-propanamide, 1,3-dihydro-N-hydroxy-β-[4-methoxy-3-(1-methylethoxy)phenyl]-1-oxo- (9CI) (CA INDEX NAME)



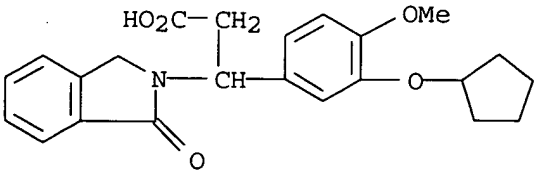
RN 333366-51-1 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N-hydroxy-5-methyl-1-oxo- (9CI) (CA INDEX NAME)



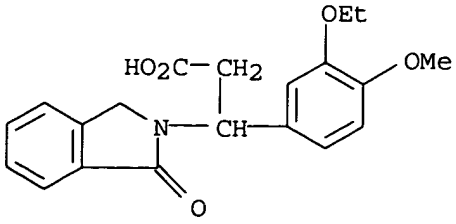
IT **167886-75-1 192819-48-0 200483-25-6**
220361-19-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of isoindolylhydroxypropionamides for reduction of tumor necrosis
factor-α levels)
RN 167886-75-1 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



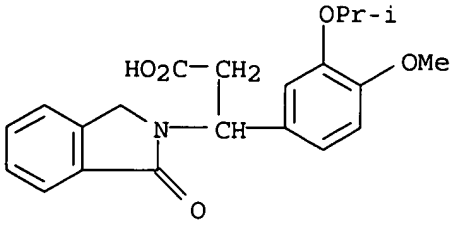
RN 192819-48-0 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



RN 200483-25-6 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



RN 220361-19-3 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, 1,3-dihydro-β-[4-methoxy-3-(1-methylethoxy)phenyl]-1-oxo- (9CI) (CA INDEX NAME)



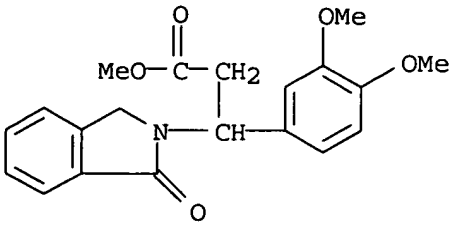
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 28 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:670337 HCAPLUS
DOCUMENT NUMBER: 134:157330
TITLE: Thalidomide analogue CC-3052 reduces HIV+ neutrophil apoptosis in vitro
AUTHOR(S): Guckian, M.; Dransfield, I.; Hay, P.; Dalgleish, A. G.
CORPORATE SOURCE: Division of Oncology, St George's Hospital Medical School, London, SW17 ORE, UK
SOURCE: Clinical and Experimental Immunology (2000), 121(3), 472-479
CODEN: CEXIAL; ISSN: 0009-9104
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Recently, water-soluble analogs of thalidomide with significantly greater immunomodulatory activity and reduced side-effects than thalidomide itself have become available. The effect of thalidomide and one analog, CC-3052, on neutrophil apoptosis was examined following culture for 20 h in vitro. Apoptosis was assessed by measuring reduced CD16 expression and Annexin V binding by flow cytometry. Neither thalidomide nor CC-3052 alone had any effect on neutrophil apoptosis when used at physiol. concns. However, when used together with PGE2 (10-7M), a potent adenylate cyclase activator, CC-3052 but not thalidomide (both 10-5M) reduced apoptosis in neutrophils from normal and HIV+ donors. The reduced apoptosis could not be attributed to the ability of CC-3052 to reduce tumor necrosis factor-α (TNF-α) production, but may have been due to its PDE4 inhibitor properties, as it increased intracellular cAMP and mimicked the effect of dibutyryl cAMP, a membrane-permeable analog of cAMP, in increasing intracellular cAMP. The results suggest a role for thalidomide analog CC-3052 in reducing the persistent activation of the TNF-α system in HIV+ patients without markedly impairing neutrophil viability.

IT **216884-02-5**, CC 3052
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(thalidomide analog CC-3052 reduction of apoptosis by neutrophils from HIV-pos. humans)

RN 216884-02-5 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 29 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:106172 HCAPLUS
DOCUMENT NUMBER: 133:26504
TITLE: The thalidomide analogue CC-3052 inhibits HIV-1 and tumor necrosis factor-alpha (TNF-α) expression in acutely and chronically infected cells in vitro
AUTHOR(S): La Maestra, L.; Zaninoni, A.; Marriott, J. B.; Lazzarin, A.; Dalgleish, A. G.; Barcellini, W.
CORPORATE SOURCE: Division of Hematology, IRCCS Ospedale Maggiore, Milan, 20122, Italy
SOURCE: Clinical and Experimental Immunology (2000), 119(1), 123-129
CODEN: CEXIAL; ISSN: 0009-9104
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

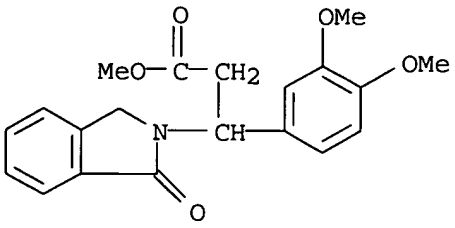
AB We investigated the in vitro effect of the water-soluble, highly stable thalidomide analog CC-3052 on HIV-1 expression and TNF-α production in latently infected promonocytic U1 cells, acutely infected T cells and monocyte-derived human macrophages (MDM), and in mitogen-stimulated ex vivo cultures from patients with primary acute HIV-1 infection. HIV-1 expression was assessed by Northern blot anal. of RNAs, and ELISA for p24 antigen release and reverse transcriptase (RT) activity. TNF-α expression was evaluated by RT-polymerase chain reaction (PCR)-ELISA for mRNA and ELISA for protein secretion. We demonstrated that CC-3052 is able to inhibit HIV-1 expression, as evaluated by mRNA, p24 release and RT activity, in phorbol myristate acetate (PMA)- and cytokine-stimulated U1 cells. Furthermore, CC-3052 inhibited HIV-1 expression, as evaluated by p24 and RT activity, in acutely infected MDM and T cells. As far as TNF-α is concerned, CC-3052 significantly reduced TNF-α mRNA and protein secretion in PMA-stimulated U937 and U1 cells, and in PMA-stimulated uninfected and acutely infected MDM. Consistently, the addition of CC-3052 reduced TNF-α production in phytohemagglutinin (PHA) and lipopolysaccharide (LPS)-stimulated whole blood cultures from patients during the primary acute phase of HIV-1 infection. Since TNF-α is among the most potent enhancers of HIV-1 expression, the effect of CC-3052 on TNF-α may account for its inhibitory activity on HIV-1 expression. Given the well documented immunopathol. role of TNF-α and its correlation with viral load, advanced disease and poor prognosis, CC-3052 could be an interesting drug for the design of therapeutic strategies in association with anti-retroviral agents.

IT **216884-02-5**, CC 3052
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(thalidomide analog CC-3052 inhibits HIV-1 and tumor necrosis factor-alpha expression in acutely and chronically infected cells in vitro)

RN 216884-02-5 HCAPLUS

CN 2H-Isoindole-2-propanoic acid, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 30 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:420122 HCAPLUS

DOCUMENT NUMBER: 131:193916

TITLE: Differential cytokine modulation and T cell activation by two distinct classes of thalidomide analogs that are potent inhibitors of TNF-α

AUTHOR(S): Corral, Laura G.; Haslett, Patrick A. J.; Muller, George W.; Chen, Roger; Wong, Lu-Min; Ocampo, Christopher J.; Patterson, Rebecca T.; Stirling, David I.; Kaplan, Gilla

CORPORATE SOURCE: Celgene Corporation, Warren, NJ, 07059, USA

SOURCE: Journal of Immunology (1999), 163(1), 380-386
CODEN: JOIMA3; ISSN: 0022-1767

PUBLISHER: American Association of Immunologists

DOCUMENT TYPE: Journal

LANGUAGE: English

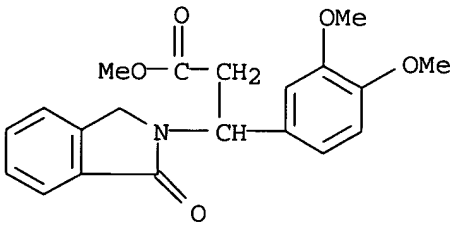
AB TNF-α mediates both protective and detrimental manifestations of the host immune response. Previous work has shown thalidomide to be a relatively selective inhibitor of TNF-α production in vivo and in vitro. Addnl., it has been recently reported that thalidomide exerts a costimulatory effect on T cell responses. To develop thalidomide analogs with increased anti-TNF-α activity and reduced or absent toxicities, novel TNF-α inhibitors were designed and synthesized. When a selected group of these compds. was examined for their immunomodulatory activities, different patterns of cytokine modulation were revealed. The tested compds. segregated into two distinct classes: one class of compds., shown to be potent phosphodiesterase 4 inhibitors, inhibited TNF-α production, increased IL-10 production by LPS-induced PBMC, and had little effect on T cell activation; the other class of compds., similar to thalidomide, were not phosphodiesterase 4 inhibitors and markedly stimulated T cell proliferation and IL-2 and IFN-γ production These compds. inhibited TNF-α, IL-1β, and IL-6 and greatly. increased IL-10 production by LPS-induced PBMC. Similar to thalidomide, the effect of these agents on IL-12 production was dichotomous; IL-12 was inhibited when PBMC were stimulated with LPS but increased when cells were stimulated by crosslinking the TCR. The latter effect was associated with increased T cell CD40 ligand expression. The distinct immunomodulatory activities of these

classes of thalidomide analogs may potentially allow them to be used in the clinic for the treatment of different immunopathol. disorders.

IT **216884-02-5**, CC 3052
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(CC 3052; differential cytokine modulation and T cell activation by thalidomide analogs as inhibitors of TNFα)

RN 216884-02-5 HCAPLUS

CN 2H-Isoindole-2-propanoic acid, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 31 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:113548 HCAPLUS
DOCUMENT NUMBER: 130:168235
TITLE: Substituted alkanohydroxamic acids and method of reducing TNFα levels
INVENTOR(S): Muller, George W.; Man, Hon-Wah
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9906041	A1	19990211	WO 1998-US15868	19980730
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2295295	AA	19990211	CA 1998-2295295	19980730
AU 9886741	A1	19990222	AU 1998-86741	19980730
AU 737008	B2	20010809		
EP 1035848	A1	20000920	EP 1998-938151	19980730
EP 1035848	B1	20030423		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
TR 200000221	T2	20000921	TR 2000-200000221	19980730

BR 9815895	A	20010116	BR 1998-15895		19980730
JP 2001511448	T2	20010814	JP 2000-504855		19980730
NZ 502379	A	20021025	NZ 1998-502379		19980730
RU 2199530	C2	20030227	RU 2000-102639		19980730
AT 238052	E	20030515	AT 1998-938151		19980730
PT 1035848	T	20030930	PT 1998-938151		19980730
ES 2196592	T3	20031216	ES 1998-938151		19980730
NO 9906529	A	20000328	NO 1999-6529		19991228
NO 315043	B1	20030630			
FI 2000000061	A	20000302	FI 2000-61		20000112
MX 200001018	A	20001110	MX 2000-1018		20000128
PRIORITY APPLN. INFO.:			US 1997-903975	A	19970731
			WO 1998-US15868	W	19980730

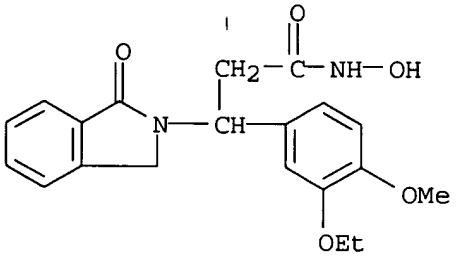
OTHER SOURCE(S): MARPAT 130:168235

AB Ioxoisoindolinylpropionamides and phthalimidopropionamidemidos were prepared and reduce the levels of TNFα and inhibit phosphodiesterase in a mammal. A typical embodiment is 3-(3-cyclopentyloxy-4-methoxyphenyl)-N-hydroxy-3-phthalimidopropionamide which was prepared by the reaction of 3-amino-(3-(3-cyclopentyloxy-4-methoxyphenyl))propionic acid and NH2OH.HCl.

IT **220360-64-5P 220360-68-9P 220360-70-3P**
220360-73-6P 220360-80-5P 220360-81-6P
220360-84-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and reduction of TNFα levels and inhibition of phosphodiesterase)

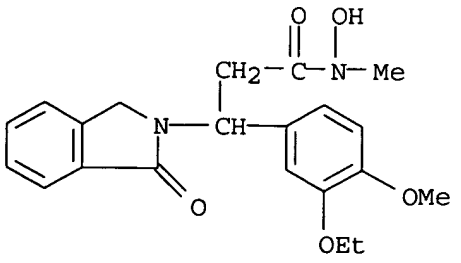
RN 220360-64-5 HCAPLUS

CN 2H-Isoindole-2-propanamide, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N-hydroxy-1-oxo- (9CI) (CA INDEX NAME)

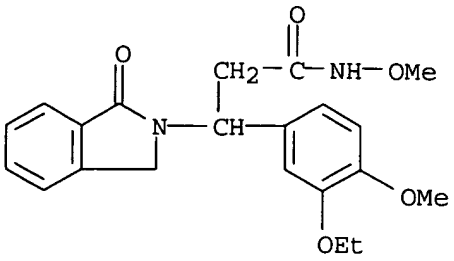


RN 220360-68-9 HCAPLUS

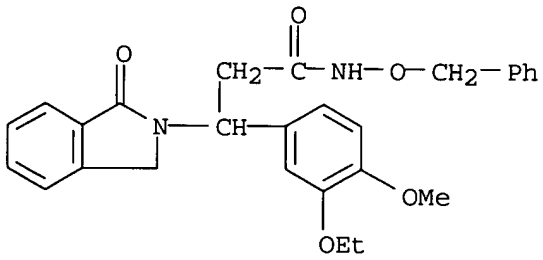
CN 2H-Isoindole-2-propanamide, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N-hydroxy-N-methyl-1-oxo- (9CI) (CA INDEX NAME)



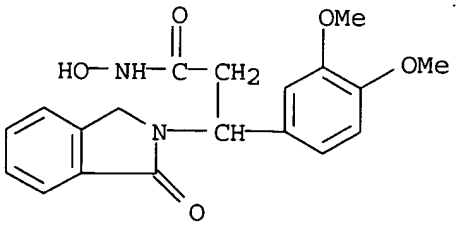
RN 220360-70-3 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-N-methoxy-1-oxo- (9CI) (CA INDEX NAME)



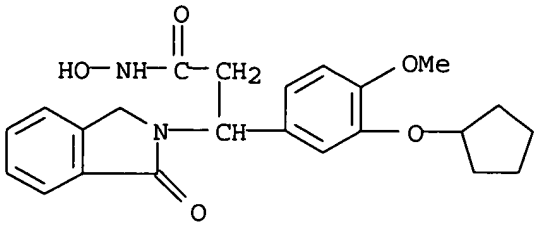
RN 220360-73-6 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-N-(phenylmethoxy)- (9CI) (CA INDEX NAME)



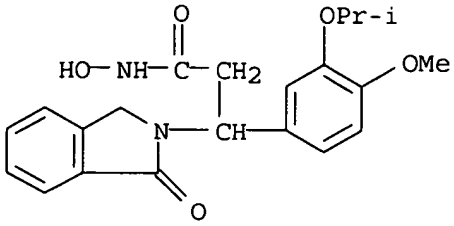
RN 220360-80-5 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-N-hydroxy-1-oxo- (9CI) (CA INDEX NAME)



RN 220360-81-6 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,3-dihydro-N-hydroxy-1-oxo- (9CI) (CA INDEX NAME)

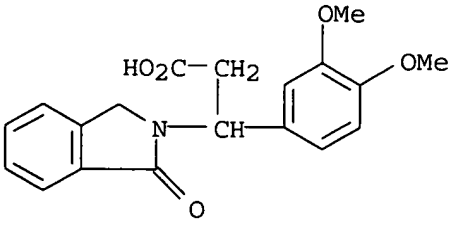


RN 220360-84-9 HCAPLUS
CN 2H-Isoindole-2-propanamide, 1,3-dihydro-N-hydroxy-β-[4-methoxy-3-(1-methylethoxy)phenyl]-1-oxo- (9CI) (CA INDEX NAME)

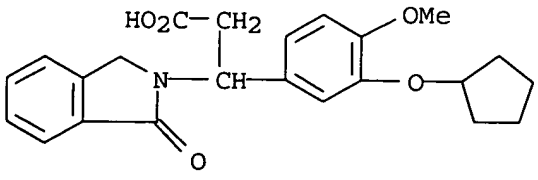


IT **167886-75-1 192819-48-0 200483-25-6**
220361-19-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant for preparation of oxoisoindolinylpropionamides/phthalimidopropionamides for reduction of TNFα levels and inhibition of phosphodiesterase)

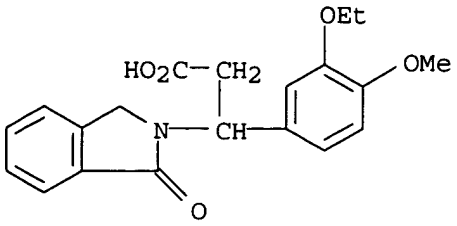
RN 167886-75-1 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



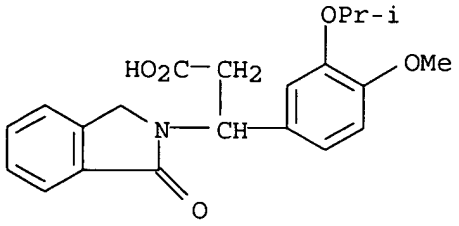
RN 192819-48-0 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



RN 200483-25-6 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



RN 220361-19-3 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, 1,3-dihydro-β-[4-methoxy-3-(1-methylethoxy)phenyl]-1-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

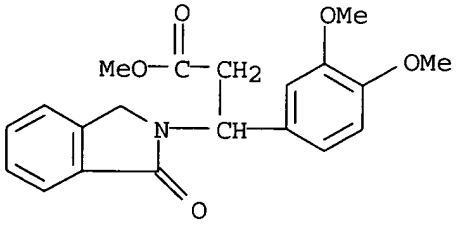
L10 ANSWER 32 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:659096 HCAPLUS
DOCUMENT NUMBER: 130:47246
TITLE: CC-3052: A water-soluble analog of thalidomide and potent inhibitor of activation-induced TNF-α production
AUTHOR(S): Marriott, J. Blake; Westby, Michael; Cookson, Sharon; Guckian, Mary; Goodbourn, Steve; Muller, George; Shire, Mary G.; Stirling, David; Dalgleish, Angus G.
CORPORATE SOURCE: Div. Oncology, St. George's Hospital Med. School, London, UK
SOURCE: Journal of Immunology (1998), 161(8), 4236-4243
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The immunomodulatory drug thalidomide has been shown to be clin. useful in a number of situations due to its ability to inhibit TNF-α synthesis. However, its use is restricted by potentially serious side effects, including teratogenicity and neurotoxicity; furthermore, insoly. may present problems in terms of systemic bioavailability. Recently, structural modifications of thalidomide have been designed enabling greatly enhanced anti-TNF-α activity in LPS-treated mice. In contrast to thalidomide (LPS-induced TNF-α IC50 .apprx.200 μM in DMSO) and other analogs tested, one of these compds., CC-3052 (IC50

.apprx.1 μM in water), is water soluble Furthermore, this analog exhibits increased stability in human plasma (t1/2 .apprx.17.5 vs. 1.5 h for thalidomide) and appears to be nontoxic, nonmutagenic, and nonteratogenic. At pharmacol. active levels, cellular proliferation and LPS-induced IL-6 mRNA and IL-12p40 mRNA (as well as IL-1β and IL-6 protein levels) in whole blood cultures were not affected; apparent inhibition of NK activity by CC-3052 was reversed upon addition of exogenous rTNF-α. In addition, IL-10 mRNA and protein levels were increased. These properties are consistent with results indicating inhibition of phosphodiesterase type IV activity by CC-3052. Furthermore, CC-3052 did not increase the degradation rate of macrophage TNF-α transcripts nor inhibit LPS-induced primary macrophage NF-κB activation. Taken together, the potency of selective TNF-α inhibition, water solubility, and increased plasma stability make CC-3052 an excellent candidate for further development and clin. evaluation for the treatment of TNF-α-mediated disease.

IT **216884-02-5**, CC 3052
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(water-soluble thalidomide analog CC-3052 as inhibitor of activation-induced TNF-α production)

RN 216884-02-5 HCAPLUS

CN 2H-Isoindole-2-propanoic acid, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 33 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:186516 HCAPLUS
DOCUMENT NUMBER: 128:230243
TITLE: Preparation of 3-phthalimido-3-(3-cyclopentyloxy-4-methoxyphenyl)propionamide and related compounds as immunotherapeutic agents
INVENTOR(S): Muller, George W.; Shire, Mary
PATENT ASSIGNEE(S): Celgene Corp., USA
SOURCE: U.S., 10 pp., Cont.-in-part of U.S. Ser. No. 520,710.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5728844	A	19980317	US 1995-578738	19951226
US 5728845	A	19980317	US 1995-520710	19950829
CA 2230487	AA	19970306	CA 1996-2230487	19960829

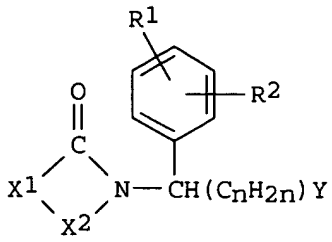
EP 957091	A1	19991117	EP 1999-200946	19960829
EP 957091	B1	20030604		
R: GB				
CZ 291613	B6	20030416	CZ 1998-609	19960829
EP 1367051	A2	20031203	EP 2003-77311	19960829
EP 1367051	A3	20031217		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PT 851857	T	20040730	PT 1996-930664	19960829
ES 2216059	T3	20041016	ES 1996-930664	19960829
CA 2241688	AA	19970703	CA 1996-2241688	19961224
WO 9723457	A1	19970703	WO 1996-US20616	19961224
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9714685	A1	19970717	AU 1997-14685	19961224
AU 723331	B2	20000824		
EP 874819	A1	19981104	EP 1996-945277	19961224
EP 874819	B1	20040526		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1206405	A	19990127	CN 1996-199413	19961224
CN 1092640	B	20021016		
JP 2000502350	T2	20000229	JP 1997-523858	19961224
RU 2174512	C2	20011010	RU 1998-113943	19961224
IL 125086	A1	20021110	IL 1996-125086	19961224
AT 267806	E	20040615	AT 1996-945277	19961224
EP 1468991	A1	20041020	EP 2004-76505	19961224
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, AL				
PT 874819	T	20041029	PT 1996-945277	19961224
ES 2222487	T3	20050201	ES 1996-945277	19961224
US 5968945	A	19991019	US 1998-7135	19980114
FI 9801437	A	19980825	FI 1998-1437	19980622
US 6180644	B1	20010130	US 1999-330701	19990611
HK 1017620	A1	20030516	HK 1999-102856	19990706
HK 1022692	A1	20031031	HK 2000-101665	20000320
US 2002002188	A1	20020103	US 2001-909506	20010720
US 6518281	B2	20030211		
US 2003114516	A1	20030619	US 2002-316673	20021211
US 2005096355	A1	20050505	US 2004-2488	20041203
US 2006003979	A1	20060105	US 2005-210693	20050825

PRIORITY APPLN. INFO.:

US 1995-520710	A2	19950829
US 1995-578738	A	19951226
EP 1996-930664	A3	19960829
EP 1996-945277	A3	19961224
WO 1996-US20616	W	19961224
US 1998-7135	A3	19980114
US 1999-366985	A1	19990804
US 2001-909506	A1	20010720
US 2002-316673	B1	20021211
US 2004-2488	B1	20041203

OTHER SOURCE(S): MARPAT 128:230243

GI



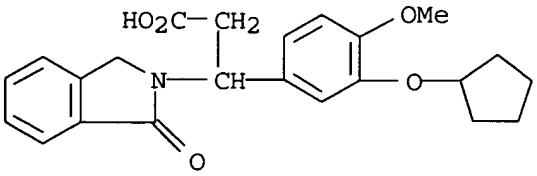
I

AB Novel amides [I; 1 of R1, R2 = R3X, the other = H, OH, NO2, alkyl, amino, cyano, CF3, alkoxycarbonyl, MeCO, R3X, etc.; R3 = C≤18 (bi)cycloalkyl, C≤18 benzocycloalkyl; X = CC bond, CH2O; X1 = (un)substituted o-phenylene; X2 = CO, CH2, CH2CO; Y = COR3, cyano, OR4, alkyl, aryl; R3 = NH2, OH, etc.; R4 = H, alkyl; n = 0-4] are inhibitors of TNFα and phosphodiesterase (no data) and can be used for treatment of cachexia, endotoxic shock, retrovirus replication, asthma, and inflammatory conditions. For example, condensation of 10.0 g 3-cyclopentyloxy-4-methoxybenzaldehyde with 4.72 g CH2(CO2H)2 in the presence of 7.00 g NH4OAc in 30 mL EtOH gave 58% 3-amino-3-(3-cyclopentyloxy-4-methoxyphenyl)propionic acid which (2.34 g) was stirred for 3 h with 1.9 g N-carbethoxyphthalimide and 0.96 g Na2CO3 in a mixture og 20 mL H2O and 20 mL MeCN under N to give 85% 3-phthalimido derivative This (2.05 g) was stirred for 1.5 h under N with 0.91 g 1,1'-carbonyldiimidazole and a trace of 4-dimethylaminopyridine in 20 mL THF, the mixture was treated with 1.07 mL of 28-30% NH4OH and the whole stirred for 1.5 h to give 49% of the title compound (m. 165-166°).

IT **192819-48-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and esterification with MeOH; preparation of 3-phthalimido-3-(3-cyclopentyloxy-4-methoxyphenyl)propionamide and related compds. as immunotherapeutic agents)

RN 192819-48-0 HCAPLUS

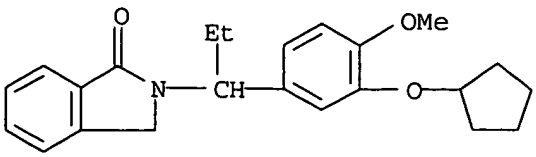
CN 2H-Isoindole-2-propanoic acid, β-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



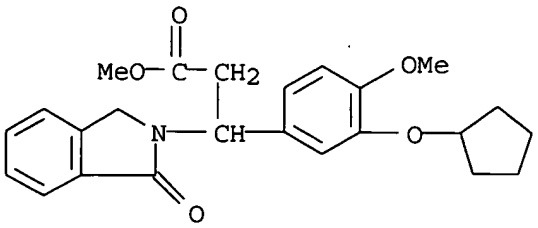
IT **192819-45-7P 192819-49-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3-phthalimido-3-(3-cyclopentyloxy-4-methoxyphenyl)propionamide and related compds. as immunotherapeutic agents)

RN 192819-45-7 HCAPLUS

CN 1H-Isoindol-1-one, 2-[1-[3-(cyclopentyloxy)-4-methoxyphenyl]propyl]-2,3-dihydro- (9CI) (CA INDEX NAME)



RN 192819-49-1 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,3-dihydro-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 34 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:15705 HCAPLUS
DOCUMENT NUMBER: 128:106406
TITLE: Immunotherapeutic imides/amides
INVENTOR(S): Muller, George W.; Shire, Mary; Stirling, David I.
PATENT ASSIGNEE(S): Celgene Corp., USA
SOURCE: U.S., 14 pp., Cont.-in-part of U.S. Ser. No. 366,667, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5703098	A	19971230	US 1996-759788	19961203
EP 797437	A1	19971001	EP 1995-940063	19951120
EP 797437	B1	20010418		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
HU 77978	A2	19990128	HU 1997-1842	19951120
RU 2164514	C2	20010327	RU 1997-112903	19951120
AT 200621	E	20010515	AT 1995-940063	19951120
ES 2155537	T3	20010516	ES 1995-940063	19951120
PT 797437	T	20010731	PT 1995-940063	19951120
CZ 290372	B6	20020717	CZ 1997-2035	19951120
PL 185101	B1	20030228	PL 1995-321071	19951120
CA 2273002	AA	19980611	CA 1997-2273002	19971203
WO 9824763	A2	19980611	WO 1997-US22369	19971203
WO 9824763	A3	19980806		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR,				

KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG,
US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
GN, ML, MR, NE, SN, TD, TG

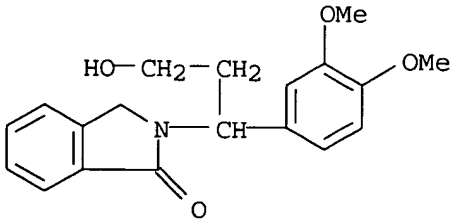
AU 9855945	A1	19980629	AU 1998-55945		19971203
AU 735540	B2	20010712			
EP 942902	A2	19990922	EP 1997-952302		19971203
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
CN 1254333	A	20000524	CN 1997-180323		19971203
NZ 336713	A	20010223	NZ 1997-336713		19971203
JP 2001506611	T2	20010522	JP 1998-525844		19971203
RU 2177471	C2	20011227	RU 1999-113849		19971203
FI 9901187	A	19990716	FI 1999-1187		19990525
PRIORITY APPLN. INFO.:			US 1994-366667	B2	19941230
			WO 1995-US15119	W	19951120
			US 1996-759788	A	19961203
			WO 1997-US22369	W	19971203

OTHER SOURCE(S): MARPAT 128:106406

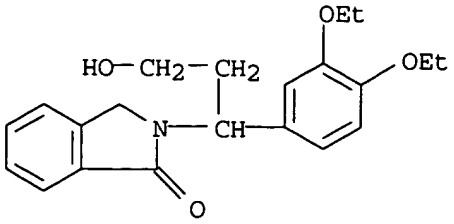
AB Imide/amide ethers and alcs. are inhibitors of cytokines including tumor necrosis factor α and can be used to combat cachexia, endotoxic shock, arthritis, asthma, and retrovirus replication. A typical embodiment is 3-phthalimido-3-(3',4'-dimethoxyphenyl)propan-1-ol (I). I was prepared by treating 3-amino-3-(3',4'-dimethoxyphenyl)-1-propanol with phthalic anhydride. Formulations for tablets, capsules, and injections containing active ingredients are provided.

IT **201408-21-1 201408-23-3 201408-24-4**
201408-26-6 201408-27-7 201408-28-8
201408-29-9 201408-33-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of imides and amides as cytokine inhibitors)

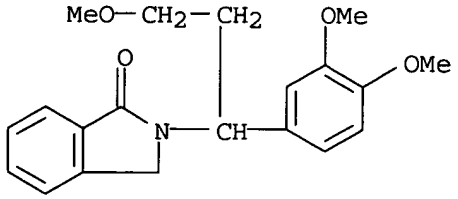
RN 201408-21-1 HCAPLUS
CN 1H-Isoindol-1-one, 2-[1-(3,4-dimethoxyphenyl)-3-hydroxypropyl]-2,3-dihydro- (9CI) (CA INDEX NAME)



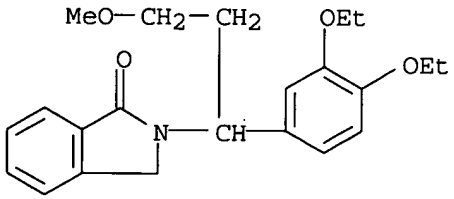
RN 201408-23-3 HCAPLUS
CN 1H-Isoindol-1-one, 2-[1-(3,4-diethoxyphenyl)-3-hydroxypropyl]-2,3-dihydro- (9CI) (CA INDEX NAME)



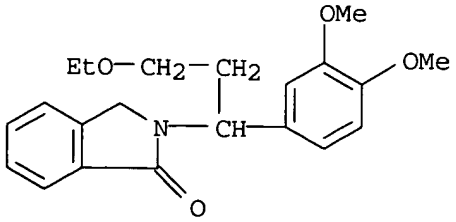
RN 201408-24-4 HCAPLUS
CN 1H-Isoindol-1-one, 2-[1-(3,4-dimethoxyphenyl)-3-methoxypropyl]-2,3-dihydro- (9CI) (CA INDEX NAME)



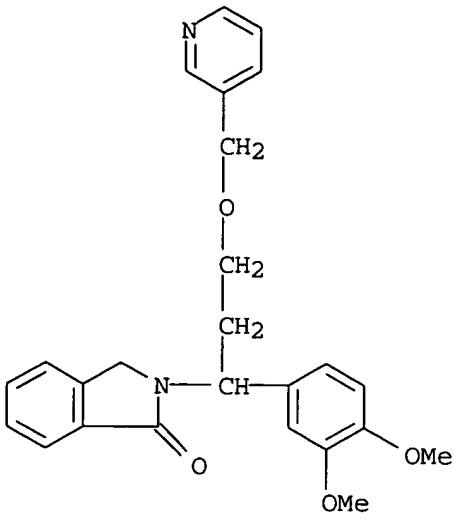
RN 201408-26-6 HCAPLUS
CN 1H-Isoindol-1-one, 2-[1-(3,4-diethoxyphenyl)-3-methoxypropyl]-2,3-dihydro- (9CI) (CA INDEX NAME)



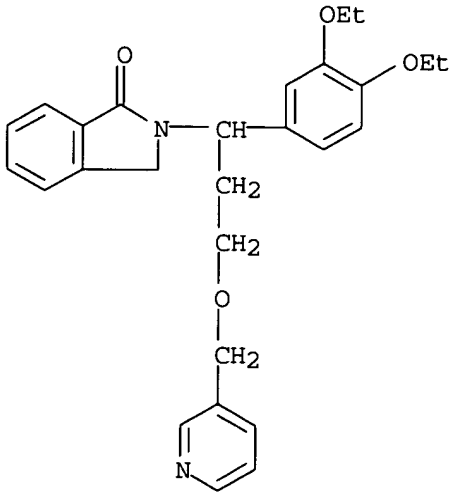
RN 201408-27-7 HCAPLUS
CN 1H-Isoindol-1-one, 2-[1-(3,4-dimethoxyphenyl)-3-ethoxypropyl]-2,3-dihydro- (9CI) (CA INDEX NAME)



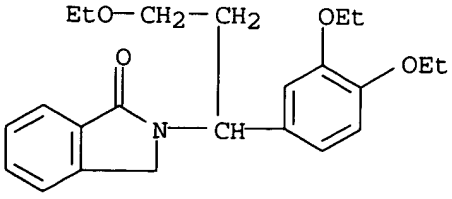
RN 201408-28-8 HCAPLUS
CN 1H-Isoindol-1-one, 2-[1-(3,4-dimethoxyphenyl)-3-(3-pyridinylmethoxy)propyl]-2,3-dihydro- (9CI) (CA INDEX NAME)



RN 201408-29-9 HCAPLUS
CN 1H-Isoindol-1-one, 2-[1-(3,4-diethoxyphenyl)-3-(3-pyridinylmethoxy)propyl]-2,3-dihydro- (9CI) (CA INDEX NAME)

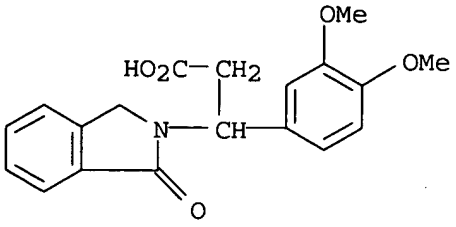


RN 201408-33-5 HCAPLUS
CN 1H-Isoindol-1-one, 2-[1-(3,4-diethoxyphenyl)-3-ethoxypropyl]-2,3-dihydro- (9CI) (CA INDEX NAME)



IT **167886-75-1**

RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of imides and amides as cytokine inhibitors)
RN 167886-75-1 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)

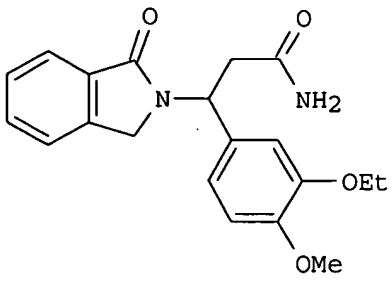


L10 ANSWER 35 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:1310 HCAPLUS
DOCUMENT NUMBER: 128:75298
TITLE: Cyclic amides
INVENTOR(S): Muller, George W.
PATENT ASSIGNEE(S): Celgene Corp., USA
SOURCE: U.S., 25 pp., Cont.-in-part of U.S. 5,605,914.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5698579	A	19971216	US 1996-703708	19960827
US 5463063	A	19951031	US 1993-140237	19931020
US 5605914	A	19970225	US 1994-258587	19940610
EP 1004580	A2	20000531	EP 2000-200491	19940701
EP 1004580	A3	20021002		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
EP 1004581	A2	20000531	EP 2000-200492	19940701
EP 1004581	A3	20020814		
EP 1004581	B1	20040922		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
EP 1004572	A2	20000531	EP 2000-200498	19940701
EP 1004572	A3	20021002		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
EP 1477486	A2	20041117	EP 2004-77075	19940701
EP 1477486	A3	20041215		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
US 5877200	A	19990302	US 1997-920715	19970829
US 6075041	A	20000613	US 1998-158612	19980922
US 6200987	B1	20010313	US 2000-547085	20000411
US 2003144325	A1	20030731	US 2003-337602	20030106
PRIORITY APPLN. INFO.:			US 1993-87510	B2 19930702
			US 1993-140237	A2 19931020
			US 1994-258587	A2 19940610
			EP 1994-921439	A3 19940701
			EP 2000-200492	A3 19940701
			US 1996-703708	A3 19960827

US 1997-920715	A3	19970829
US 1998-158612	A3	19980922
US 1999-230389	A3	19990507
US 2000-543809	A1	20000406
US 2001-781179	A1	20010212

OTHER SOURCE(S): MARPAT 128:75298
GI

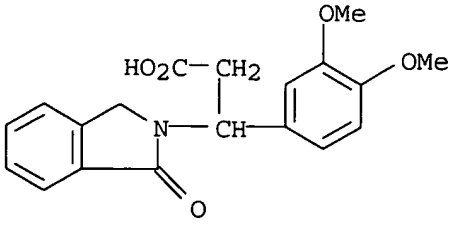


I

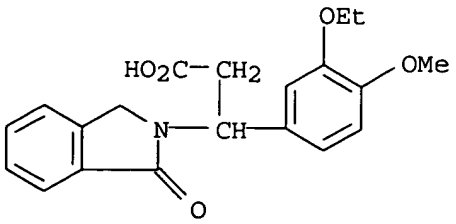
AB Cyclic amides such as I are prepared Thus, I was prepared in 2 steps starting from 3-amino-3-(3-ethoxy-4-methoxyphenyl)propionic acid and phthalaldehyde.

IT **167886-75-1P 200483-25-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(cyclic amides as potential tumor necrosis factor inhibitors)

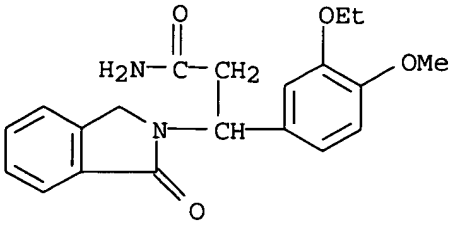
RN 167886-75-1 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



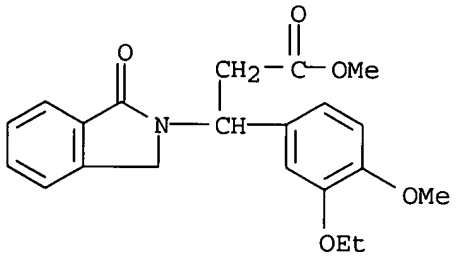
RN 200483-25-6 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



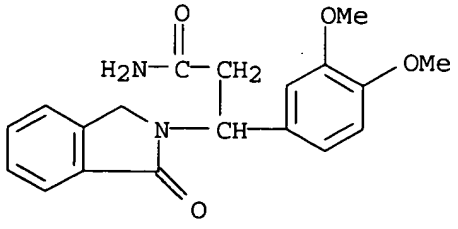
IT **188684-83-5P 200483-34-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(cyclic amides as potential tumor necrosis factor inhibitors)
RN 188684-83-5 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



RN 200483-34-7 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



IT **167886-76-2P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cyclic amides as potential tumor necrosis factor inhibitors)
RN 167886-76-2 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



L10 ANSWER 36 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:506832 HCAPLUS
DOCUMENT NUMBER: 127:121630
TITLE: Preparation of imides as PDE III, PDE IV and THF

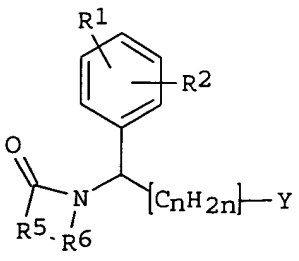
inhibitors
INVENTOR(S): Muller, George W.; Shire, Mary
PATENT ASSIGNEE(S): Celgene Corporation, USA; Muller, George W.; Shire, Mary
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9723457	A1	19970703	WO 1996-US20616	19961224
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5728844	A	19980317	US 1995-578738	19951226
AU 9714685	A1	19970717	AU 1997-14685	19961224
AU 723331	B2	20000824		
EP 874819	A1	19981104	EP 1996-945277	19961224
EP 874819	B1	20040526		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2000502350	T2	20000229	JP 1997-523858	19961224
RU 2174512	C2	20011010	RU 1998-113943	19961224
IL 125086	A1	20021110	IL 1996-125086	19961224
AT 267806	E	20040615	AT 1996-945277	19961224
FI 9801437	A	19980825	FI 1998-1437	19980622
HK 1017620	A1	20030516	HK 1999-102856	19990706

PRIORITY APPLN. INFO.:

US 1995-578738	A	19951226
US 1995-520710	A2	19950829
WO 1996-US20616	W	19961224

OTHER SOURCE(S): MARPAT 127:121630
GI



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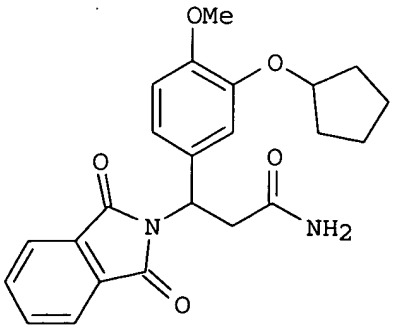


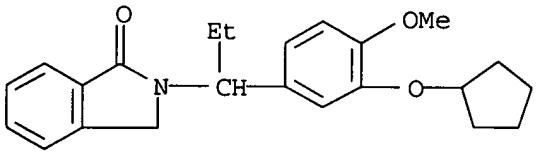
II

AB The title compds. [I; one of R1 and R2 = R3X and the other = H, NO2, CN,

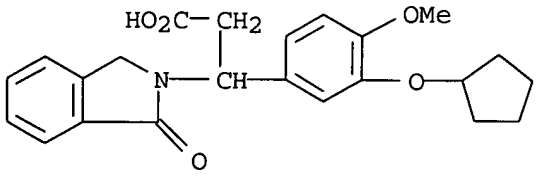
etc; (R3 = monocycloalkyl, bicycloalkyl, etc.; X = a bond, CH2, O, N); R5 = (un)substituted o-phenylene, vicinally divalent residue of pyridine, pyrrolidine, etc.; R6 = CO, CH2, CH2CO; Y = COZ, lower alkyl, aryl, etc.; Z = NH2, OH, OCH2Ph, etc.; n = 0-3], inhibitors of TNFα, phosphodiesterase and NF-κB activation which can be used to combat cachexia, endotoxic shock, retrovirus replication, asthma, and inflammatory conditions, were prepared and formulated. Thus, reaction of 3-cyclopentyloxy-4-methoxybenzaldehyde with malonic acid in the presence of AcONH4 in EtOH followed by reaction of the resulting 3-amino-3-(3-cyclopentyloxy-4-methoxyphenyl)propionic acid with N-carbethoxyphthalimide in the presence of Na2CO3 in H2O/MeCN, and treatment of 3-phthalimido-3-(3-cyclopentyloxy-4-methoxyphenyl)propionic acid with NH4OH in the presence of 1,1'-carbonyldiimidazole and DMAP in THF afforded 3-phthalimido-3-(3-cyclopentyloxy-4-methoxyphenyl)propionamide (II).

IT **192819-45-7P 192819-48-0P 192819-49-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of imides as PDE III, PDE IV and THF inhibitors)

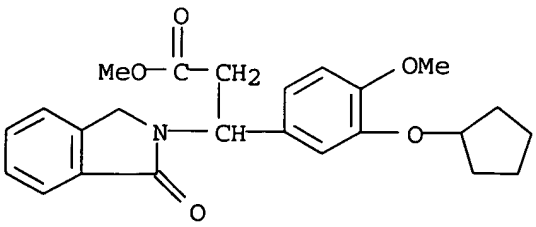
RN 192819-45-7 HCAPLUS
CN 1H-Isoindol-1-one, 2-[1-[3-(cyclopentyloxy)-4-methoxyphenyl]propyl]-2,3-dihydro- (9CI) (CA INDEX NAME)



RN 192819-48-0 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



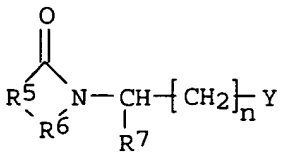
RN 192819-49-1 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,3-dihydro-1-oxo-, methyl ester (9CI) (CA INDEX NAME)



L10 ANSWER 37 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:276450 HCAPLUS
DOCUMENT NUMBER: 126:251071
TITLE: Preparation of novel heterocyclylalkanenitriles as inhibitors of tumor necrosis factor α
INVENTOR(S): Muller, George W.; Shire, Mary
PATENT ASSIGNEE(S): Celgene Corporation, USA; Muller, George W.; Shire, Mary
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9708143	A1	19970306	WO 1996-US14077	19960829
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
US 5728845	A	19980317	US 1995-520710	19950829
CA 2230487	AA	19970306	CA 1996-2230487	19960829
AU 9669632	A1	19970319	AU 1996-69632	19960829
AU 716775	B2	20000309		
EP 851857	A1	19980708	EP 1996-930664	19960829
EP 851857	B1	20040218		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
EP 957091	A1	19991117	EP 1999-200946	19960829
EP 957091	B1	20030604		
R: GB				
JP 2000500118	T2	20000111	JP 1997-510629	19960829
NZ 318212	A	20010525	NZ 1996-318212	19960829
RU 2196134	C2	20030110	RU 1998-105689	19960829
CZ 291613	B6	20030416	CZ 1998-609	19960829
EP 1367051	A2	20031203	EP 2003-77311	19960829
EP 1367051	A3	20031217		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
AT 259787	E	20040315	AT 1996-930664	19960829
PT 851857	T	20040730	PT 1996-930664	19960829
SK 284144	B6	20041005	SK 1998-272	19960829
ES 2216059	T3	20041016	ES 1996-930664	19960829
FI 9800038	A	19980224	FI 1998-38	19980109
HK 1022692	A1	20031031	HK 2000-101665	20000320
PRIORITY APPLN. INFO.:			US 1995-520710 A	19950829
			EP 1996-930664 A3	19960829
			WO 1996-US14077 W	19960829

OTHER SOURCE(S): MARPAT 126:251071
GI



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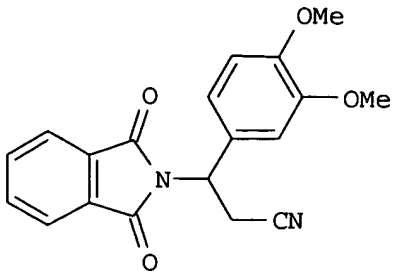


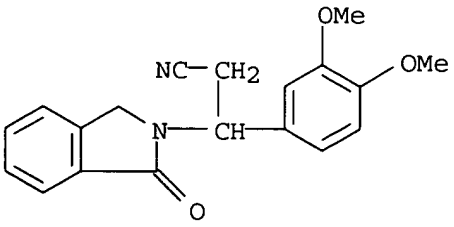
II

AB The title compds. [I; Y = CN, C(O)(CH2)mMe (wherein m = 0-3); R5 = (un)substituted o-phenylene, a divalent C4-10 cycloalkyl, etc.; R6 = CO, CH2, CH2CO, SO2; R7 = C1-12 alkyl, C4-12 cyclic or bicyclic alkyl, etc.; n = 0-3], inhibitors of tumor necrosis factor α and phosphodiesterases, particularly PDE III and PDE IV, and can be used to combat cachexia, endotoxic shock, retrovirus replication, asthma, and inflammatory conditions, were prepared and formulated. Thus, dehydratation of 3-phthalimido-3-(3,4-dimethoxyphenyl)propionamide with SOCl2 in the presence of 4-methylmorpholine in DMF afforded 79% the title compound II. Compds. I are effective at 1-1000 mg/day.

IT **188684-79-9P 188684-80-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel heterocyclylalkanenitriles as inhibitors of tumor necrosis factor α)

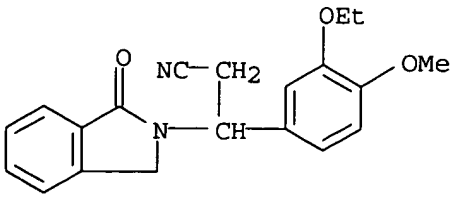
RN 188684-79-9 HCAPLUS

CN 2H-Isoindole-2-propanenitrile, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



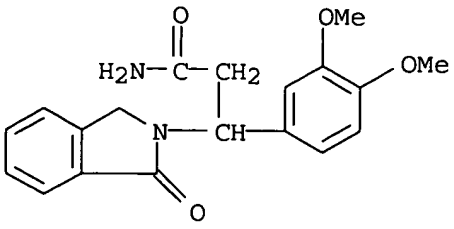
RN 188684-80-2 HCAPLUS

CN 2H-Isoindole-2-propanenitrile, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)

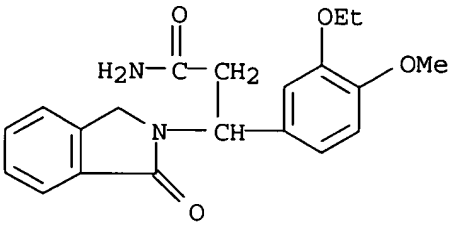


IT **167886-76-2 188684-83-5**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of novel heterocyclylalkanenitriles as inhibitors of tumor necrosis factor α)

RN 167886-76-2 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



RN 188684-83-5 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3-ethoxy-4-methoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



L10 ANSWER 38 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:169160 HCAPLUS
DOCUMENT NUMBER: 126:199454
TITLE: Preparation of cyclic imides as inhibitors of tumor necrosis factor α
INVENTOR(S): Muller, George W.
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: U.S., 22 pp., Cont.-in-part of U.S. Ser. No. 87,510, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5605914	A	19970225	US 1994-258587	19940610
US 5463063	A	19951031	US 1993-140237	19931020
EP 1004580	A2	20000531	EP 2000-200491	19940701
EP 1004580	A3	20021002		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
EP 1004581	A2	20000531	EP 2000-200492	19940701
EP 1004581	A3	20020814		

EP 1004581	B1	20040922			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE					
EP 1004572	A2	20000531	EP 2000-200498	19940701	
EP 1004572	A3	20021002			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE					
EP 1477486	A2	20041117	EP 2004-77075	19940701	
EP 1477486	A3	20041215			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE					
US 5698579	A	19971216	US 1996-703708	19960827	
US 5877200	A	19990302	US 1997-920715	19970829	
US 6075041	A	20000613	US 1998-158612	19980922	
US 6200987	B1	20010313	US 2000-547085	20000411	
US 2003144325	A1	20030731	US 2003-337602	20030106	
PRIORITY APPLN. INFO.:			US 1993-87510	B2 19930702	
			US 1993-140237	A2 19931020	
			US 1994-258587	A2 19940610	
			EP 1994-921439	A3 19940701	
			EP 2000-200492	A3 19940701	
			US 1996-703708	A3 19960827	
			US 1997-920715	A3 19970829	
			US 1998-158612	A3 19980922	
			US 1999-230389	A3 19990507	
			US 2000-543809	A1 20000406	
			US 2001-781179	A1 20010212	

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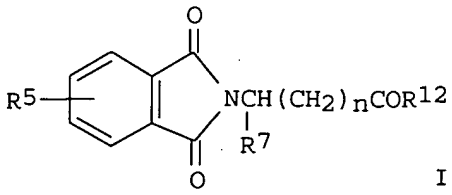

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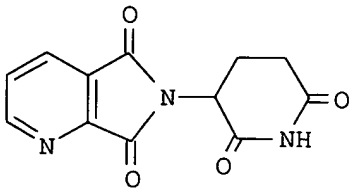

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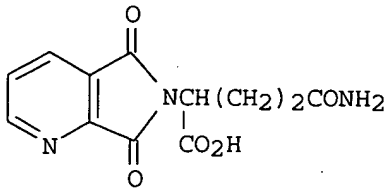


III

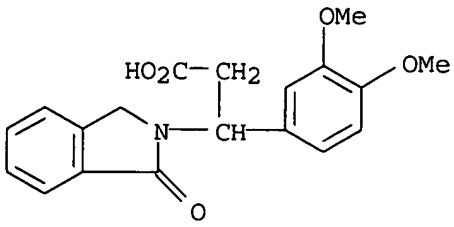
AB Cyclic imides, such as I [R5 = H, NO2, CN, CF3, CO2Et, CO2Me, CO2Pr, Ac, CONH2, AcO, CO2H, OH, NH2, alkyl, alkoxy, halo; R7 = pyridyl, substituted Ph, (un)substituted benzyl, naphthyl, benzyloxy, imidazol-4-ylmethyl; R12 = amino, OH, ester; n = 0-3], are inhibitors of tumor necrosis factor α and can be used to combat cachexia, endotoxic shock, and retrovirus replication. Thus, I (R5 = H, R7 = 4-MeOC6H4, R12 = NH2, n = 1) was prepared from 3-(4-MeOC6H4)CH(NH2)CH2CO2H and N-(carboethoxy)phthalimide via amidation of the phthalimidopropionic acid. Also, 2-(2,6-dioxo-3-piperidinyl)-4-azaisoindoline-1,3-dione (II) was prepared from L-glutamine and 2,3-pyridinedicarboxylic anhydride via intramol. cyclization of glutaramic acid III.

IT **167886-75-1P**

RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use);

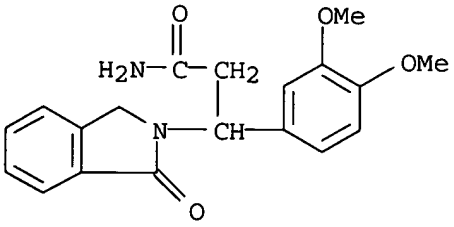
BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of cyclic imides as inhibitors of tumor necrosis factor α)

RN 167886-75-1 HCAPLUS
CN 2H-Isoindole-2-propanoic acid, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



IT **167886-76-2P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyclic imides as inhibitors of tumor necrosis factor α)

RN 167886-76-2 HCAPLUS
CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



L10 ANSWER 39 OF 39 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:797249 HCAPLUS
DOCUMENT NUMBER: 123:198617
TITLE: Imides as inhibitors of TNF alpha
INVENTOR(S): Muller, George W.
PATENT ASSIGNEE(S): Celgene Corp., USA
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9501348	A2	19950112	WO 1994-US7411	19940701
WO 9501348	A3	19950309		

W: AU, CA, CZ, FI, HU, JP, KR, NZ, PL, RU, SK, UA, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

CA 2166315	AA	19950112	CA 1994-2166315	19940701
AU 9472167	A1	19950124	AU 1994-72167	19940701
AU 687843	B2	19980305		
EP 706521	A1	19960417	EP 1994-921439	19940701
EP 706521	B1	20021002		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09500872	T2	19970128	JP 1995-503648	19940701
HU 75312	A2	19970528	HU 1996-3	19940701
EP 1004580	A2	20000531	EP 2000-200491	19940701
EP 1004580	A3	20021002		
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EP 1004581	A2	20000531	EP 2000-200492	19940701
EP 1004581	A3	20020814		
EP 1004581	B1	20040922		
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EP 1004572	A2	20000531	EP 2000-200498	19940701
EP 1004572	A3	20021002		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
PL 180377	B1	20010131	PL 1994-312386	19940701
RU 2174516	C2	20011010	RU 1996-102001	19940701
AT 225344	E	20021015	AT 1994-921439	19940701
PT 706521	T	20030228	PT 1994-921439	19940701
ES 2184765	T3	20030416	ES 1994-921439	19940701
AT 277036	E	20041015	AT 2000-200492	19940701
EP 1477486	A2	20041117	EP 2004-77075	19940701
EP 1477486	A3	20041215		
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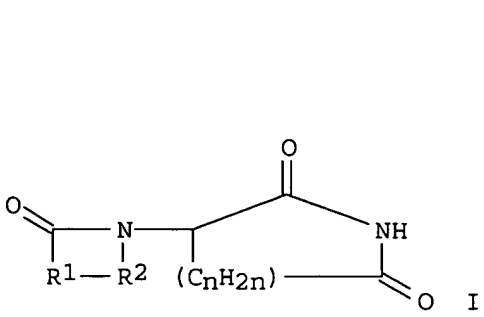
CZ 294444	B6	20050112	CZ 2003-663	19940701
PT 1004581	T	20050131	PT 2000-200492	19940701
ES 2226696	T3	20050401	ES 2000-200492	19940701
FI 9506362	A	19960226	FI 1995-6362	19951229
FI 114984	B1	20050215		
US 6476052	B1	20021105	US 2000-633908	20000807
HK 1025769	A1	20050408	HK 2000-104989	20000810
US 2003144325	A1	20030731	US 2003-337602	20030106
FI 2004000593	A	20040427	FI 2004-593	20040427

PRIORITY APPLN. INFO.:	US 1993-87510	A	19930702
	EP 1994-921439	A3	19940701
	EP 2000-200492	A3	19940701
	WO 1994-US7411	W	19940701
	US 1996-690258	A1	19960724
	US 1996-701494	A1	19960822
	US 1997-48278P	P	19970530
	WO 1997-US13375	A1	19970724
	US 1999-230389	B3	19990507
	US 2000-543809	A1	20000406
	US 2001-781179	A1	20010212

OTHER SOURCE(S): MARPAT 123:198617
GI



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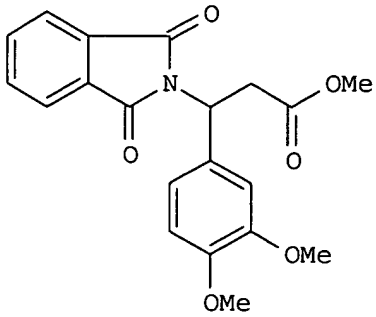

II

AB A variety of cyclic imides and certain acyclic analogs and/or precursors are inhibitors of tumor necrosis factor α (no data) and can be used to combat cachexia, endotoxic shock, and retrovirus replication. One subgroup of the compds. is I [R1 = divalent residue of 3,4-pyridine, pyrrolidine, imidazole, naphthalene, thiophene, or C2-6 alkane (un)substituted by (un)substituted Ph; R2 = CO, SO2; n = 1-3]. A typical embodiment from a different subgroup is Me 3-phthalimido-3-(3,4-dimethoxyphenyl)propionate, i.e. II, which was prepared from 3,4-(MeO)2C6H3CH(NH2)CH2CO2H by conversion to the Me ester hydrochloride with SOCl2 and MeOH (66%) and reaction of this with N-(carboethoxy)phthalimide in the presence of Na2CO3 in aqueous MeCN (92%). A total of 93 synthetic examples and 6 formulations are given.

IT **167886-75-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of cyclic imides and analogs as TNF-α inhibitors)

RN 167886-75-1 HCAPLUS

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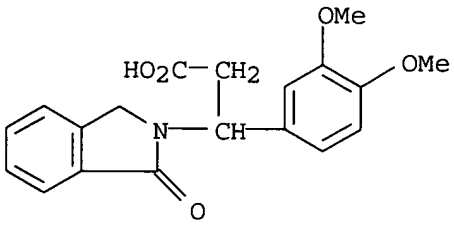
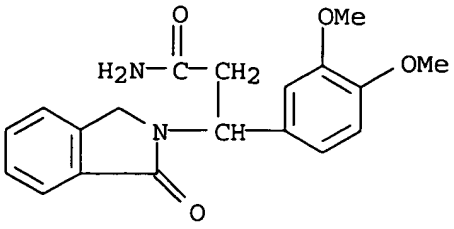


IT **167886-76-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of cyclic imides and analogs as TNF-α inhibitors)

RN 167886-76-2 HCAPLUS

CN 2H-Isoindole-2-propanamide, β-(3,4-dimethoxyphenyl)-1,3-dihydro-1-oxo- (9CI) (CA INDEX NAME)



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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	255.35	592.56

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-35.25	-35.25

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